Principal Investigator: **Tejas Patil, MD**
COMIRB No: **16-2025**
Version Date: **October 20, 2020**
Study Title: *ARM Study: A phase II trial to evaluate crizotinib in the neoadjuvant setting in non-small cell lung cancer patients with surgically resectable, ALK, ROS1, or MET-oncogene positive non-small cell lung cancer*

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you do not understand before deciding whether or not to take part.

Why is this study being done?

This study plans to learn more about non-small cell lung cancer (NSCLC) by testing blood and tumor tissue samples. We will be studying a chemotherapy drug called crizotinib, which is already used to treat certain types of NSCLC, but we are trying to learn if patients who are given this treatment before they have surgery (neoadjuvant) to remove their tumor tissue may respond better to this treatment. We will collect plasma and tumor tissue samples before you start the treatment with crizotinib, at the time of surgery, and after your surgery. Evaluation of tumor tissue early in treatment will allow us to study early cancer cell activity

You are being asked to be in this research study because you have been newly diagnosed with NSCLC with the specific gene mutations ALK, ROS1 or MET mutation that your doctor believes meets the requirements to be in the study.

Crizotinib (Xalkori ®) will be called “the study drug” throughout the rest of this consent form.

Other people in this study

Up to 260 people from your area will participate in the study.

Up to 260 people around the country will be in the study.

What happens if I join this study?

If you join the study, you will be asked to sign this consent form before you receive any study related tests or procedures. You will be given a copy to keep and the original form will be kept at the clinic. You can withdraw from the study at any time and without giving a reason. This will not affect the standard medical care you receive.

There are three parts to this study:

1. Before starting the study (Screening)
2. During the Study (Treatment)
3. Completion of Study (After Treatment Follow-up)

This next section is an overview of what will be expected of you, and what you can expect if you take part in this study.

Study Procedures:

Some procedures you receive while taking part in this study are "standard care procedures" for treatment of your disease. Some procedures are required only for this study and are called "research" procedures. All procedures that will take place during this study are described below. The time points when these study procedures will take place are specified in the next section called "Study Visits".

- **Informed Consent**
  Before any study required procedure takes place, this informed consent document will be discussed with you and you will be given a copy of this document.

- **Medical and Cancer History**
  Before you start the study, we will record your date of birth, race, ethnicity, complete medical history. This history will look at the background and progress of your cancer and the prior therapies you have received for your disease.

- **Physical Examination**
  A physical examination will be completed as part of your standard of care. We will also look at whether the study drug is affecting your body functions including lungs, heart, abdomen, extremities, skin, head (eyes, ears, noses, hair, etc.), and neurologically.

- **Blood samples**
  These tests are sometimes referred to as safety labs so the study doctor can be sure it is safe for you to take part in this study and to be given the study drugs.
  - Serum pregnancy tests will be performed in women who are able to become pregnant. A positive pregnancy test prior to being given the study drugs, will exclude you from starting or continuing to take part in the study.
  - Complete blood count (CBC)
  - Comprehensive metabolic panel (CMP)

- Tumor DNA testing. The cost of this test is paid for by this study.

- **Tumor tissue biopsy**
  When you have a biopsy a sample of your tumor tissue is removed from your body. Some of this tissue will undergo routine pathologic evaluation, but some tissue will be leftover and normally discarded. For this research, we will test some of the leftover tissue. The cost of this test will be paid for by this study. There will be two time points where we will test your tumor tissue for this research, once at the beginning of the study to see if you are eligible to take part in the study, and then to compare after surgical removal of the tumor tissue. If you had a previous biopsy we will ask to use some of the tumor tissue that was leftover (archived tumor tissue), or we will use the leftover tumor tissue from the biopsy that will be performed before your surgery.

- **Electrocardiogram (ECG)**
  An ECG is a test that records the electrical activity of the heart.

- **Positron emission tomography (PET)**
  A PET scan is a radiation or nuclear medicine image that will show 3-dimensional, color images of your body.

- **Brain MRI scan**
  An MRI is a scan that uses radio waves and a strong magnetic field to provide images of internal organs and tissues.

- **Vital Signs**
  We will take your blood pressure, heart rate, respiratory rate, body temperature and weight. Height will be measured only during screening.

- **Performance Status**
  We will assess how well you are performing your daily activities.

- **Other Medications**
  Your study doctor will let you know which other medications you can and cannot take while taking part in this study. From the time you first receive the study drugs through 30 days after the last dose, we will record other medications you may be taking.

- **Review Adverse Events**
  Some risks have been identified because of the disease process or through use of the study drugs. These are commonly called side effects and will be followed very closely by your doctor and the study staff. More information about these will be provided in the Risk section of this consent form.

Study Visits:

1. SCREENING

- Sign Informed Consent
- Medical history and physical exam
- Performance status assessments
- Review of medications
- Blood draws – about 1-2 Tablespoons of blood will be drawn
  - CBC
  - CMP
  - Pregnancy test (for women of childbearing potential)
  - Tumor DNA evaluation – **research**
- ECG
- Molecular testing on diagnostic biopsy
- PET scan
- Brain MRI – if clinically indicated

2. TREATMENT

Day 1 to Day 42

- Crizotinib 250mg is taken by mouth two times per day from Day 1 to Day 42 – **research**

Day 21 *(+/- 4 days)*

- History and physical exam
- Performance status assessments
- Review of medications
- Review of adverse events
- Blood draws - about 1 Tablespoon of blood will be drawn
  - CBC
  - CMP
- ECG

Day 42 *(+/- 4 days, but before surgery)*

- History and physical exam
- Performance status assessments
- Review of medications
- Review of adverse events
- Blood draws - about 1 Tablespoon of blood will be drawn
  - CBC
  - CMP
  - circulating tumor DNA evaluation - **research**
- PET scan

Day 43-49

- Surgery to remove tumor
- Molecular testing of tissue – **research**

3. AFTER TREATMENT FOLLOW-UP

- Standard of care visits with your physician, including routine surveillance scans, medical history and physical exam.
- You will have the option to participate in additional blood draws for further circulating tumor DNA evaluation after your routine scans. This is an **optional research** procedure.

How long will I be on the study?

You will receive treatment with the study drug for 42 days before your surgery to remove your tumor tissue. Any treatment you receive after your surgery will not be part of this study. However, we will continue to follow your progress for up to 5 years by reviewing your medical chart.

What are the possible discomforts or risks?

Risks from the Study Drug – crizotinib

As with any study drug, side effects may occur when taking this study drug. While taking part in this study, and being treated with the study drugs, you will be watched carefully for any side effects. Some side effects may go away after you stop taking the study drug. Some side effects can be long lasting and may never go away or may even lead to death.

You should talk to your study doctor about any side effects or discomfort you may have. The study doctor may give you some medicine that will help with some side effects. The study doctor may also interrupt or discontinue the study drug.

You will be notified by your study doctor of any new side effects seen in other patients that occur during the time you are on the study. This may affect you wanting to continue in this research study.

Based on animal studies and/or other studies with similar types of drugs, side effects or discomforts you may experience while in this study include**:**

Common Side Effects

- Changed or blurry vision
- Nausea
- Feeling tired or fatigued
- Diarrhea
- Constipation
- Abdominal pain
- Low white blood cell count, which may increase your risk of infection
- Low heart rate or longer than normal recharge of heart between beats
- Dizziness
- Vomiting
- Loss of appetite
- Swelling in arms or legs
- Change in taste
- Numbness or tingling of arms and legs
- Elevated liver enzymes

Uncommon Side Effects

- Low red blood cell count (anemia), which may make you feel tired or fatigued
- Upset stomach or indigestion
- Stomach/throat ulcers
- Flu-like symptoms
- Muscle spasms
- Headache
- Skin rash
- Interstitial lung disease or pneumonitis
- Liver damage

Risks of Having Blood Taken

In this study we will need to get about 3 tablespoons of blood from you. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

Risks of having an ECG

An electrocardiogram (ECG) is a test that records the electrical activity of the heart. Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.

Risks of having a PET Scan

PET stands for positron emission tomography, which uses radiation. The machine detects pairs of gamma rays that are emitted indirectly by a tracer (positron-emitting radionuclide), which is placed in the body on a biologically active molecule. The images are reconstructed by computer analysis. These are not painful but if a patient is uncomfortable with small confined spaces or noise sensitive, they should alert their physician. There may be related procedures that might be uncomfortable.

Risks of Having an MRI

In this study we will take Magnetic Resonance Images (MRI's) of your head. The MRI machine uses powerful magnetic waves to take pictures inside the body. The waves themselves are not harmful, but they can cause metal to heat up and electronics to stop working.

You should NOT have an MRI if you have metal or electronic devices inside your body. Heart pacemakers and insulin pumps are examples of electronic devices.

The MRI machine is a small round tube. It might make you uncomfortable if you do not like tight spaces.

The most common side effect of having an MRI is flashing lights in the eyes. This is caused by the magnetic waves and is not harmful. Some people also experience warmth and reddening of the skin. This usually goes away after a few minutes.

Risks of loss of confidentiality

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

Risks of pregnancy and breastfeeding

Women of childbearing potential should avoid becoming pregnant while taking the study drug. Women of childbearing potential who are receiving the study drug, or partners of women of childbearing potential receiving the study drug, should use adequate contraceptive methods during use of the study drug and for at least 90 days after receiving the last dose of the study drug.

There are no adequate and well-controlled studies in pregnant women using the study drug, but based on animal studies such exposure to the study drug can cause harm to a fetus. It also is not known whether the study drug is excreted in breast milk, but many drugs are excreted in breast milk, and can cause harm to nursing infants. If you are breastfeeding, you should not take part in this study.

Female participants who breastfeed or become pregnant, and male participants who impregnate a female partner, while taking the study drug need to tell your study doctor immediately so it can be reported to the study drug manufacturer. If you become pregnant while taking part in this study, you will need to withdraw from the study, but we will need to follow-up with you throughout the pregnancy and report to the study drug manufacturer the outcome of your pregnancy.

The study may include risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about Crizotinib. However, there is no guarantee that your health will improve if you join this study. Also, there could be risks to being in this study. If there are risks, these are described in the section describing the discomforts or risks.

Are there alternative treatments?

There may be other ways of treating your stage IA-IIIA non-small cell lung cancer. These other ways include:

- You may choose to receive treatment with another experimental therapy.
- You may choose to receive treatment with another approved therapy.
- You may choose to receive comfort/palliative care.
- You could also choose to get no treatment at all.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

This research is being conducted by Tejas Patil, MD, with funding support by Pfizer, Inc. who is also providing the study drug, and paying for the tumor DNA test.

The sponsor will only pay for procedures not considered standard of care as detailed below.

Will I be paid for being in the study?

You will not be paid to be in the study.

Will I have to pay for anything?

It will not cost you anything to be in the study.

You and/or your health insurance may be billed for the costs of medical care during this study, if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs, or if you do not have insurance, these costs will be your responsibility.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call Tejas Patil, MD immediately. His phone number is 720-848-9264.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Tejas Patil, MD, you may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Tejas Patil, MD at 720-848-9264. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Tejas Patil, MD with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

A description of this clinical trial will be available on http://www.clinicaltrials.gov/. This Web site will not include information that can identify you. You can search this Web site at any time.

Optional Study Procedures

Here are the optional parts of this study. ***Remember, no matter what you decide to do about these optional parts of the study, you may still take part in the main study.*** If you decide to withdraw your consent for the optional parts, you can continue to take part in the main study, unless you withdraw your consent for the main study as well.

Following each optional procedure is a statement asking if you want to participate in the optional procedure. Please read the statement and think about your choice. After reading the sentence, please check “Yes” or “No” and initial next to your choice. If you have any questions, please talk to your doctor or nurse.

1. *Optional Consent for Additional Blood Draws*

   As a participant at the University of Colorado, you are being asked if you would like to participate in **optional** blood draws during the follow-up phase of this study. If

you agree to participate, you will have blood drawn after each routine scan during the follow-up phase. Your sample will be analyzed for circulating tumor DNA. This is a **research** procedure and is paid for by the study.

I give my permission additional blood draws after each routine follow-up scan.

☐ Yes ☐ No _____Initials

2. *Optional Consent for Data and Specimen Banking for Future Research*

Dr. Patil would like to keep some of the data, blood and tissue that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about non-small cell lung cancer. The research that is done with your data and samples is not designed to specifically help you. It might help people who have non-small cell lung cancer and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Patil keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want Dr. Patil to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Patil decides to destroy them.

When your data and samples are given to other researchers in the future, Dr. Patil will not give them your name, address, phone number or any other information that will let the researchers know who you are.

Sometimes data and samples are used for genetic research (about diseases that are passed on in families). Even if your data and samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your data and samples include learning more about what causes non-small cell lung cancer and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. Patil will protect your records so that your name, address

and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by Dr. Patil.

Please read each sentence below and think about your choice. After reading each sentence, circle "yes" or "no." If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data, blood and tissue to be stored in a central tissue bank at University of Colorado Biorepository for future use by the study investigators:

1. I give my permissions for my data, blood and tissue samples to be kept by Dr. Patil for use in future research to learn more about how to prevent, detect, or treat lung cancer.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my data, blood and tissue samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   ☐ Yes ☐ No _____Initials

3. I give my permission for my archived tumor tissue, if available, to be used for future research.

   ☐ Yes ☐ No _____Initials

4. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Tejas Patil, MD
University of Colorado Denver, Anschutz Medical Campus
Division of Medical Oncology
Mail Stop 8113 HSC
12631 E. 17th Avenue
Academic Office One (AO1), Room 8515
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- Pfizer, Inc. who is the company providing funding support and study drug Crizotinib for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research.

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals, but we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* **of the following health information about you collected in this study available to:** Guardant Health (the company analyzing the tumor DNA in your blood), and other participating sites in this study.

Some of the research procedures involve genetic testing or the use of your genetic information. Your genetic information will not be released to others.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)

- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Tissue samples and the data with the samples.
- Billing or financial information

What happens to Data, Tissue, Blood and Specimens that are collected in this study?

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures

In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

Some of these optional procedures may involve genetic testing or the use of your genetic information. Your genetic information will not be released to others.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature: _____ Date: _____

Print Name: _____

Consent form explained by: _____ Date: _____

Print Name: _____

A signature line for a witness is required for consent of non-reading subjects and consent using a short form.

Witness Signature: _____ Date: _____

Witness Print Name: _____

Witness of Signature
Witness of consent process