DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
ATOMIC ARI-AT-002: Phase 2 Trial of Brigatinib after Treatment with Next-Generation ALK inhibitors in Refractory ALK Rearranged NSCLC

CONCISE SUMMARY
The purpose of this study is to test and evaluate the safety and effectiveness of an investigational drug called brigatinib (AP26113) in subjects with advanced lung cancer (called non-small cell lung cancer or NSCLC) with ALK rearrangement, who have previously received at least one line of treatment with an anti-cancer drug, and whose cancer has gotten worse.

You will be prescribed brigatinib to take orally once a day for the duration of the study. Blood samples and possibility a small piece of tissue may be required. You will also have other tests, exams and procedures for study purposes and your standard of care. If you enroll, you may continue to take brigatinib, as long as it's working, otherwise your participation will last approximately 2 years.

There are risks to this study that are described in this document. Some risks include diarrhea, headache, nausea and/or vomiting, being tired or weak, and radiation risks from CT scans.

If you are interested in learning more about this study, please continue reading below.

You are being asked to take part in this research study because you have advanced lung cancer. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Dr. Thomas Stinchcombe will conduct the study and it is funded by Takeda Pharmaceuticals. The sponsor of this study is the Academic Thoracic Oncology Medical Investigators Consortium (ATOMIC). The study is being conducted by investigators affiliated with ATOMIC and Dr. Stinchcombe is the lead investigator for the study. Duke University will be paid by this group to perform this research and these funds may reimburse part of Dr. Stinchcombe's salary. Dr. Stinchcombe serves on an advisory board for Takeda Oncology.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Stinchcombe will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

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WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test an investigational drug called brigatinib (AP26113) in subjects with advanced lung cancer (called non-small cell lung cancer or NSCLC) with ALK rearrangement.

An ALK mutation is an abnormality or mutation in a gene called ALK (anaplastic lymphoma kinase) that can occur in cancer cells such as lung cancer cells. This mutation is actually a gene rearrangement (a fusion of 2 genes) that is causing your cancer cells to grow and spread. This type of lung cancer is not very common, and people who get it are normally younger and are not smokers. Doctors do not know definitively what causes this disease, but they are searching for new and better treatments that would slow the cancer down and help people who have it feel better.

Brigatinib has been approved by the FDA for patients with metastatic non-small cell lung cancer (NSCLC) and alterations in the ALK gene whose cancer has progressed during their initial therapy.

The uses of Brigatinib in this study have not been approved by the FDA, therefore Brigatinib is considered an investigational drug. The word “investigational” means the study drug is still being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA).

The purpose of this study is to evaluate the safety and effectiveness of brigatinib in subjects with advanced lung cancer (NSCLC), with an ALK gene rearrangement, whose cancer got worse after or while taking a drug called an ALK inhibitor. ALK inhibitor drugs specifically target the abnormal ALK protein. Examples of these drugs are ceritinib (ZykadiaR) and alectinib (AlecensaR). Brigatinib also targets the ALK protein and has undergone some preliminary testing in subjects with lung cancer with ALK rearrangement. Because it also targets different mutations, it may help subjects who have progressed on or failed to respond to other ALK inhibitor drugs.

ARE THERE ANY REASONS YOU SHOULD NOT BE IN THIS STUDY?

You should not be in this study if you have received (or are receiving) chemotherapy, radiation therapy, or other investigational drugs within 7 days of the first dose of brigatinib. You should also not be in this study if you are a pregnant or breast-feeding female or are unwilling to take contraceptive drugs to prevent pregnancy during the study; have any history or presence of any lung disease; have drug-related or radiation pneumonitis (lung inflammation); have had any active significant gastrointestinal bleeding within the past 3 months or any active infection requiring intravenous antibiotics; or are unable to swallow study medication.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 120 people will take part in this study at approximately 11 different hospitals and medical facilities, and approximately 14 people will take part at Duke.

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WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign and date this consent form.
Some tests and procedures will be necessary to confirm that you meet the eligibility requirements to participate in this study.
Tests and Procedures
After you have signed the consent form, we will schedule you for a screening visit to conduct the tests and procedures necessary to see if you are eligible to participate.
If you have recently had some of the tests or procedures that are required during the screening visit, you may not need these tests or procedures repeated. The study doctor and members of the study team will talk to you about what tests will be necessary. Additionally, all of these tests and procedures may not occur on the same day but are required prior to determining whether or not you can be in the study.

The following tests and procedures will occur during this visit and will be used to confirm that you are eligible for the study:

- Physical Examination along with height and weight and a complete medical history
- Vital signs (blood pressure, heart rate, temperature, respirations)
- Review of how well you perform daily tasks
- Routine blood laboratory tests – approximately 2 tablespoons of blood (CBC, platelet count, and serum chemistries)
- Serum pregnancy test for women of childbearing potential (7 days prior to receiving study drug).
- Testosterone level if male
- Electrocardiogram (ECG) to see how well your heart is functioning
- CT Scan (Computed Tomography) of your chest, abdomen and pelvis to look at the extent of your cancer
- MRI (Magnetic Resonance Imaging) of your brain to see if your cancer may have spread to this area.
- Tumor sample (from a previous biopsy when you were taking an ALK inhibitor drug). If no previous tumor sample is available, you will need to have a new biopsy performed in order to participate in this study, unless it cannot be performed with minimal risk (no deep tissue biopsies would be performed, such as lung biopsies).
- Review of all medications (including any herbal or nutritional supplements) you may be taking. Please bring all medications, vitamins, and supplements that you are taking to this visit for review.

If after all screening tests and procedures your study doctor determines that you are eligible for participation in the study, you will come to the clinic for your first visit. This is considered Cycle 1 Day 1. A cycle consists of 28 days. You will be given a medication diary to record each use of your study medication. The study team will collect and review this diary during your clinic visits. You must also bring your empty bottle or remaining pills with you to each visit.

During this study, you will be placed in Cohort A or Cohort B depending on what other treatment you have received for your cancer. Subjects in both Cohorts A and B will receive the study medication,

brigatinib, at a dose of 90 mg. It is to be taken by mouth once a day for the first 7 days of Cycle 1 followed by 180 mg by mouth once a day, continuously, thereafter.
OR

If you were previously treated with brigatinib, prior to this study, and your cancer has gotten worse, or if your cancer has gotten worse while you have been on this study but you are tolerating the current dose well, you may be eligible for Cohort C. Cohort C subjects will receive brigatinib at a dose of 240mg to be taken by mouth daily.

Subjects who are currently in Cohorts A and B and have disease progression, will be asked to read and sign a separate consent addendum, called "beyond progression" if interested in continuing in the study.

Your doctor and your dosing diary will tell you your dose and the number of tablets per dose.
Study Regimen Procedures
All Cycles, Day 1 (Every 28 days) plus or minus 2 days
The following tests and procedure will be done during each cycle visit every 28 days as follows:

- Physical examination and weight
- Measure vital signs (blood pressure, heart rate, temperature, respirations)
- Review how well you perform your daily tasks and activities
- Review any signs and symptoms you may be experiencing
- Routine blood laboratory tests – approximately 2 tablespoons of blood (CBC, platelet count, and serum chemistries)
- Research Blood Sample for ctDNA - to see how the study drug may work in someone who has previously taken drugs called ALK inhibitors (Cycle 1, Day 1 and Day 1 of every odd cycle- 3, 5, etc.). Your genes are made up of DNA. DNA is short for deoxyribonucleic acid. A gene, or DNA, contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. ctDNA is DNA from your tumor that can be detected in your blood sample. About 2 tablespoons of blood will be collected each time.
- Review all medications you may be taking
- Receive study drug brigatinib and new diary
- Review & collect medication diary
- Collect empty medication bottle or remaining pills

Cycle 1, Day 8 plus or minus 2 days

- Measure vital signs (blood pressure and heart rate)
- Review any signs and symptoms you may be experiencing
- Routine blood laboratory tests – approximately 2 tablespoons of blood (CBC, platelet count, and serum chemistries)
- Review all medications you may be taking
- Review your medication diary

If your study doctor feels it is appropriate, after 7 days, and on day 8 of Cycle 1, the study doctor will increase your dose of brigatinib to 180mg.

If you were treated with brigatinib, prior to this study, your dose will not change on Cycle 1 Day 8, if you are tolerating your current dose well.

In addition to the tests and procedures done during each cycle visit, the following additional tests will occur on odd numbered cycles (1,3,5,7 and so forth) as outlined below:

Cycles 3, 5 and Every Odd Numbered Cycle thereafter on Day 1, plus or minus 2 days

- Research Blood Sample for ctDNA - to see how the study medication may work in someone who has previously taken drugs called ALK inhibitors
- Testosterone level if male
- MRI (Magnetic Resonance Imaging) of your brain to see if your cancer may have spread to this area. This will be done if you have known brain metastases or if it is needed for your care (clinically indicated).
- CT Scan (Computed Tomography) of your chest and abdomen to look at the extent of your cancer. A CT scan of the pelvis will be done as well if there is evidence that the disease has spread to that region.

After the study drug has been stopped for any reason, we will ask you to come back in 30 days for a final visit, where you will have the following tests and/or procedures:

Visit at End of Study Drug Regimen (30 days, plus or minus 3 days)

- Physical examination and weight
- Measure vital signs (blood pressure, heart rate, temperature, respirations)
- Review how well you perform your daily tasks and activities
- Review any signs and symptoms you may be experiencing
- Routine blood laboratory tests – approximately 2 tablespoons of blood (CBC, platelet count, and serum chemistries)
- Research Blood Sample for ctDNA - to see how the study medication may work in someone who has previously taken drugs called ALK
- Optional biopsy to obtain tumor sample:

Optional Tumor Biopsy at Progression:

You will be asked if you are willing to undergo a biopsy to provide new samples of tumor tissue at the end of study if your tumor(s) has progressed. A biopsy would only be done if you have tumor in an accessible area (such as on the skin or a superficial lymph node). No biopsies that would entail significant risk would be done (for example, deep tissue biopsies such as lung biopsies). The site of the biopsy will not be the same in every subject and it will depend on where you have superficial tumor located. Your doctor will discuss the location of the biopsies, the procedure, and the risks with you in detail.

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THIS BIOPSY IS COMPLETELY OPTIONAL AND YOU CAN STILL PARTICIPATE IN THIS STUDY IF YOU DO NOT AGREE TO THE BIOPSY. This sample of your tumor will help researchers identify if there are any mutations causing resistance. You can change your mind at any time and withdraw your consent to the biopsy.

A biopsy of tumor tissue may be taken by cutting out the entire tumor nodule or by taking a biopsy with a hollow needle (called a core biopsy). In some cases, a smaller needle procedure (called a fine needle aspirate) may be enough.

If you have a biopsy for your routine care (not for research), you also have the option to provide a tumor tissue sample.

Please initial and date your choice below:

_____Yes, I will provide a biopsy and understand that I can change my mind and withdraw my consent:

_____No, I decline to provide the biopsy:

After you have completed this study, you will come to clinic for your long-term standard of care follow-up every 3 months for up to two 2 years. This may be able to be done by review of your medical records. This can be discussed with your study doctor.

USE OF TISSUE FOR FUTURE RESEARCH
Biological samples collected for the study will be shipped and stored in the research laboratories at the University of Colorado until the completion of the study. If there is tumor tissue remaining after study specific tests are completed, you are being asked to give permission for the remaining tissue to be stored and used for future research on lung cancer.

If you do not wish to allow your samples to be used for future research, you should initial "no" in the boxes below. You are not required to agree to the use of your samples for future research. If you choose to provide your samples, they will be used to conduct research tests that may help the study sponsor find out if certain types of cancer respond better to treatment than others and may improve future treatment options for patients with lung cancer. Because the field of science is always advancing, we cannot predict all the tests that will be done. If you agree to provide your samples, they will be kept indefinitely.

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Some data about your disease will be linked to the samples. These data may be used by researchers, including your diagnosis, disease history, prior treatments, age, gender, and race. Your data will be de-identified so that researchers will not know who you are.

It is unlikely that what is learned from these future research studies will have a direct benefit to you.

Because all information and samples will be coded, it will not be possible to share any test results with you or your study doctors. There are no plans to provide financial compensation to you.

Please place your initials next to "Yes" or "No" for the question below:

My tumor sample(s) may be stored, used and disclosed for future research as described above.

_____ Yes _____ No
Initials Initials

HOW LONG WILL I BE IN THIS STUDY?
This study involves an initial screening visit (which might last 4-8 hours) to determine if you are eligible to be in the study. If after screening you are eligible for participation and are enrolled in the study, you will come to clinic for approximately 7 clinic visits that may last 2-4 hours to be followed for safety monitoring and to see if the study drug is working. If the study drug is working, you may continue for as long as you receive benefit or until you decide to stop the study. After you have stopped taking study drug, you will be asked to do a final visit for safety. Follow up will consist of coming to clinic every 3 months for routine standard of care visits for up to 2 years or until you choose to stop the study completely. This may be able to be done by review of your medical records. This can be discussed with your study doctor at your end of the study regimen visit.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE POSSIBLE REASONS THAT I CAN BE REMOVED FROM THE STUDY OR THE STUDY MIGHT END?
- Your disease progresses while on study
- You experience a deterioration of your condition
- Requirement for other anti-tumor therapy
- Non-compliance to taking the study drug in accordance with instructions provided
- Pregnancy
- Death

- Lost to follow up
- Any other reason that, in the opinion of your physician, justifies your removal
- Sponsor terminates the study for any reason

WHAT ARE THE RISKS OF THE STUDY?
We cannot know the side effects of brigatinib ahead of time. Some of the side effects could be serious or even cause death in rare circumstances, and allergic reactions could happen in some people. Brigatinib may interfere with other drugs that you are taking, or vice versa. You should tell your Study Doctor about any changes in your health that develop while you are in this study.

During the study you may have discomforts and risks from brigatinib or from the study procedures. Discomforts and risks may vary from person to person. Although we do not know when all the discomforts and/or risks may happen, all patients participating in the study will be carefully watched for side effects.

It is possible you may experience no discomfort, some, or many discomforts. It is also possible there is risk of a rare or previously unknown side effect that may be mild or severe and can be life-threatening or fatal. You must tell your Study Doctor any side effects that you experience. Please notify your Study Doctor of any visual changes experienced during the treatment course. Your Study Doctor may give you treatment to ease the undesirable effects. Your Study Doctor may also stop the study treatment if you have a severe reaction to brigatinib. You will be monitored closely for all side effects.

The following list of side effects (all grades) which may be associated with brigatinib have been seen with the use of brigatinib.

Very common (reported in more than 10% of patients) included:
- Low levels of red blood cell count (which can cause you to feel tired)
- Low levels of a type of white blood cells, including white blood cells called neutrophils and lymphocytes (which could increase the risk of infection)
- Activated partial thromboplastin time (APTT) increased (mean a lack of or low level of one of the blood clotting factors or another substance needed to clot blood)
- High blood sugar levels
- White blood cell count decreased
- Decreased appetite
- Low levels of sodium in the blood
- Low levels of potassium in the blood
- Low levels of magnesium in the blood
- Low levels of phosphate in the blood
- Headache

- Peripheral neuropathy, a condition in which nerves outside the brain and spinal cord (peripheral nerves) have been damaged which can result in symptoms such as numbness, tingling, prickling sensation, or pain
- Dizziness
- Visual Disturbance
- High Blood Pressure
- Cough
- Shortness of breath
- Pneumonitis (inflammation of the lung) or Interstitial lung disease (ILD), diseases that affect the lungs
- Nausea
- Diarrhea
- Vomiting
- Constipation
- Abdominal pain
- Increased liver enzymes (Aspartate aminotransferase (AST) increased or Alanine
- (ALT) increased) which can suggest damage to the liver
- Increased lipase level (an enzyme measured in the blood that reflects function of the pancreas; elevations in lipase may indicate inflammation of the pancreas)
- Increased amylase level (an enzyme measured in the blood that reflects function of the pancreas; elevations in amylase may indicate inflammation of the pancreas)
- Increased alkaline phosphatase level, an enzyme in the blood produced by the liver and other organs
- Rash includes dermatitis acneiform (appearance similar to acne), erythema (redness of the skin), exfoliative rash (redness and peeling of the skin), rash erythematous (redness of the skin or mucous membranes, caused by increased blood flow in superficial blood vessels), rash macular or rash maculo- papular (a type of rash characterized by a flat, red area on your skin that is covered with small connected bumps)
- Itchy skin
- Increased creatine phosphokinase level (an enzyme measured in the blood, elevations may indicate injury or stress to muscle tissue, the heart, or the brain)
- Muscle pain
- Muscle spasms, an involuntary contraction of a muscle, which usually resolve quickly but are often painful
- Joint Pain
- Fatigue or tiredness
- Edema (buildup of fluid in the body which causes the affected tissue to become swollen)

Common (reported in 1-10% of patients) included:

- Decreased platelet count (a decrease in platelets, a component of blood whose function is to stop bleeding by clumping and clotting blood vessel injuries)
- Unable to obtain an adequate amount or quality of sleep
- Distortion of the sense of taste
- Electrocardiogram QT prolonged (a change in ECG, a study of the electrical system of the heart that may indicate an increased risk of serious abnormalities in the heart's rhythm)
- Slow heart rate
- Noticeably rapid, strong, or irregular heartbeats
- Dry mouth
- Stomatitis (inflammation of the lining of any of the structures in the mouth, including cheeks, gums, tongue, lips, throat and roof or floor of the mouth)
- Indigestion or upset stomach
- Dry skin
- Musculoskeletal chest pain
- Pain in extremity
- Fever
- Non-cardiac chest pain

Because brigatinib shares some features with other drugs already being investigated for non-small cell lung cancer and other cancers, it is possible that it will cause similar side effects to those drugs. These include visual disturbances, testosterone level decrease, inflammation of lung tissue which can be fatal, and liver dysfunction which can be fatal. Symptoms of liver dysfunction can include weakness, fatigue, anorexia, nausea, vomiting, abdominal pain, yellowing of the skin, dark urine, generalized itching, and can cause many complications including excessive bleeding.
Brigatinib may cause side effects that we cannot know about ahead of time, some of which could be serious or even cause death in rare circumstances.
You will be monitored closely for these side effects. If you develop symptoms, your doctors will give you the care that you need. You must tell the study doctor about any new health problems that develop while you are in the study.

Reproductive Risks

It is not known what effects brigatinib has on human pregnancy or development of the embryo or fetus. Therefore, female patients participating in this study should avoid becoming pregnant, and male patients should avoid impregnating a female partner.

For Women
If you are a woman who could possibly become pregnant (you have not completed menopause, or you have not had a hysterectomy and/or both tubes and/or both ovaries removed), and you have a partner

who is able to father children, a blood pregnancy test (using 1 teaspoon of blood drawn from a vein by needle stick) will be performed and it must be negative before you can continue in this study. In women 40 years old and older, blood pregnancy tests can sometimes give a false positive or indeterminate result, and additional testing may be required to confirm your eligibility.

You and your partner must agree to either abstain completely from vaginal intercourse for the time you sign this consent form until 4 months after the last dose of study drug, or agree to use a highly effective method of contraception for the same length of time. Brigatinib may decrease effectiveness of hormonal contraceptives, so birth control pills, implants, injections, patches, or vaginal rings are not allowed in this study. Highly effective methods that are allowed include (a) partner vasectomy, (b) bilateral tubal ligation, or (c) intrauterine devices IUDs). If you and your partner are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required by this study.

Women should abstain from egg donation, from the time of screening to at least 4 months after the last dose of study drug.

Because no method of birth control is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant. If pregnancy is confirmed, the study doctor will stop your study drugs but continue to follow you during the pregnancy to better understand the potential effects of brigatanib on developing pregnancies.

For Men
The effects of brigatanib on developing pregnancies that began while the father was taking the drug are not known. In addition, brigatanib may be transmitted in semen to a partner during sexual activity. If you have a partner who could possibly become pregnant (she has not completed menopause, or she has not had a hysterectomy and/or both tubes and/or both ovaries removed), you must agree to either abstain completely from vaginal intercourse from the time you sign this consent form until 4 months after the last dose of study drug, or agree to use a condom every time you have intercourse, even if you have had a vasectomy (because a vasectomy does not prevent transmission of drug in semen). If your partner is currently pregnant, becomes pregnant, or is breastfeeding, you should use a condom for all types of intercourse. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should promptly notify her doctor. She will be asked for permission to follow the pregnancy to better understand the potential effects of brigatanib on developing pregnancies.

Men should not donate sperm from the time of screening until 4 months after the last dose of study drug

No human data on the effect brigatinib on fertility are available. Based on reproductive studies in male animals, brigatinib may cause reduced fertility in males. The clinical relevance of these findings to

human fertility is unknown. If you are concerned about future fertility, your study doctor will discuss options for fertility preservation with you.

Risks of Radiation:
You may have a number of CT scans and MRI scans that are part of the regular care for your condition, and you would have them whether or not you participate in this research. These studies will not add to the risk of the research. However, if you have concerns about the overall radiation exposure or MRI safety issues, you should discuss them with your physician.
A possible health problem seen with radiation exposure is the development of cancer later in life. This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research may range from about one in 2,000 to about one in 1,000. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all.
We can compare this possible extra cancer risk to other risks (over a lifetime) that everyone is subject to in everyday life. For example, the chances of a person dying of cancer with no extra radiation exposure are about one in 4. The chances of dying in a car crash are about one in 82, and the chances of being killed by a car while crossing the street are about one in 730.

MRI:
MRI uses a magnet and radio waves to make images (pictures) of the inside of the head and/or body. There have been no ill effects reported from exposure to the magnetism or radio waves used for these studies; however, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal that may cause injury to you. We will ask you about metal within your body (this includes certain dyes used in tattoos and body piercings). If there is any question about potentially hazardous metal within the body, you will not be able to have an MRI study. We will also keep the MR room locked so that no one carrying metal objects enters the room while you are having this scan performed. In addition, the MR scanner makes a loud buzzing noise that could affect hearing ability. You will be provided with earplugs and assistance in their use in order to protect your hearing. You will be able to communicate with the scanner technologist using an intercom and/or signaling device. The technologist will try to help you feel as comfortable as possible in the scanner. You can ask to stop the scan and be removed from the scanner at any time by using the intercom or signaling device

Risks of Tumor Biopsies:
The biopsy site will depend on where you have superficial tumor located (in the skin or in a lymph node). Your study doctor will discuss this and the specific risks of the biopsy with you at the time of the procedure.

A biopsy of the skin or lymph node is generally a non-hazardous procedure, but as with any procedure, there are risks and discomforts. For example, you may feel some amount of pain or discomfort during

the biopsy, including slight stinging pain when a local anesthetic is injected by needle to numb the area, pressure and dull pain where a biopsy needle or punch is inserted, discomfort from lying still for an extended time, and/or soreness at the biopsy site. Possible hazards may include: 1) reaction to the anesthetic (numbing medicine), 2) excessive bleeding at the needle injection site or from the surgical incision, 3) redness, bruising and swelling, 4) infection and 5) excessive scarring.
While the local numbing medicine xylocaine is almost entirely free from allergic properties (such as causing hives), an allergic reaction is possible, and you will not be given xylocaine if you have a history of such a reaction. The xylocaine will be given by a small injection into the skin at the site of the biopsy.
To speed healing, one or two stiches (also known as sutures) will be placed, which will be removed 5-7 days later. During the healing process, you will be asked to keep the biopsy site clean and dry, and to apply antibiotic ointment. Infection rarely occurs and is largely prevented by the use of an aseptic (or sterile) biopsy technique and proper wound care. If infection does occur, you will be instructed to keep the wound clean and to apply warm, wet compresses for 15 minutes, three times a day, until the infection subsides. If the infection persists, antibiotics may be prescribed.
Any complications arising from the biopsy may be treated with observation, additional medications, or in some cases, additional surgery. The study doctor will discuss the specific risks of the biopsy with you at the time of the procedure.

Risks of Drawing Blood:
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Drug and Food Interactions:
Other medications may be harmful to take with brigatinib. Brigatinib may interfere with other drugs you need or other drugs you take may interfere with brigatinib. For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study. Talk to your study doctor if you take any herbal medications (St. John‘s Wort, Blue Cohash, Estroven, etc.) and grapefruit-containing products. These medications may interact with brigatinib.

You may not receive any other anticancer medication while on this study.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
Research studies are designed to obtain new knowledge. If you agree to take part in this study, there may be direct medical benefit to you. It is possible that your tumor could shrink temporarily, but that cannot be guaranteed. We hope that in the future the information learned from this study will benefit other people with your condition.

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WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Instead of being in this study, you have the following alternatives: standard of care treatment for your type of lung cancer, palliative care (treatment of your symptoms only), or no treatment. Please talk to your doctor about these and perhaps other options (other investigational approaches).

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to ATOMIC and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, representatives and affiliates of ATOMIC, the Duke University Health System Institutional Review Board, the Duke Cancer Institute, the National Cancer Institute, the Duke Office of Audit, Risk and Compliance (OARC), and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.

As part of this study, you will be asked to have certain tests, x-rays, and/or procedures performed. Some of these tests, x-rays and/or procedures would have been done as part of your regular care. The study doctor will use these test results both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to representatives and affiliates of ATOMIC. Results of tests and studies done solely for this research study and not as part of your regular care will not be included in your medical record.

Study information, your study number, and samples collected as part of this study will be included in secure electronic trial systems. These systems may be managed and monitored by companies who work with the Sponsor.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law

designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

The study results will be retained in your research record forever. Any research information in your medical record will also be kept indefinitely.

This information may be further disclosed by the sponsor of this study, ATOMIC. If disclosed by the sponsor, the information is no longer covered by the federal privacy regulations.

If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

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.

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

WHAT ARE THE COSTS?
You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the

study with Dr. Stinchcombe. At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

The study sponsor, ATOMIC, has agreed to pay for services and procedures that are done solely for research purposes. Please talk with the PI/study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible.

We will monitor your DUHS patient care charges to make sure that costs are directed appropriately. If you have any questions or concerns about appropriate billing, contact your study team coordinator so that he/she can help find a resolution.

ATOMIC will provide the study drug/biologic free of charge to you. If you decide to withdraw from the study before it ends, your study doctor may request that you return for a checkup before you stop your study drug if he thinks that stopping it suddenly may harm you and may ask you to complete the tests that would ordinarily occur when a person completes the study.

Please ask the research staff if you would like to know more about which tests and studies are being done solely for research purposes.

WHAT ABOUT COMPENSATION?
You will not be paid for taking part in this research study.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

If you are injured as a direct result of the Study Drug or any properly performed procedures required by the Protocol, the study sponsor, Academic Thoracic Oncology Medical Investigators Consortium, will reimburse you or the provider of services for the reasonable and necessary costs of diagnosis and treatment you receive for your injuries provided all aspects of the study protocol have been followed correctly and the injuries are not the result of the natural progression of your underlying or pre-existing conditions or events, unless made worse by your participation in the study.

For questions about the study or research-related injury, contact Dr. Thomas Stinchcombe at (919) 681-6509 during regular business hours and at (919) 970-2829 after hours and on weekends and holidays.

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
ATOMIC ARI-AT-002: Phase 2 Trial of Brigatinib after Treatment with Next-Generation ALK inhibitors in Refractory ALK Rearranged NSCLC

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or institution.

If you do decide to withdraw, we ask that you contact Dr. Stinchcombe in writing and let him know that you are withdrawing from the study. His mailing address is:

Dr. Thomas Stinchcombe
Duke University Medical Center
Morris Building, DUMC, PO Box 3198
30 Medicine Circle
Durham, North Carolina 27710

In addition, you must return all unused study drug to Dr. Stinchcombe or his staff.
Dr. Stinchcombe may ask you to complete the tests that would ordinarily occur when a person completes the study.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at anytime without your consent. If this occurs, you will be notified and your study doctor will discuss other options with you.

For withdrawal of samples: If you want to withdraw your samples from storage, you must contact your study doctor, Dr. Thomas Stinchcombe, in writing and let him know you are withdrawing your permission for your samples to be stored. His mailing address is stated above.

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
ATOMIC ARI-AT-002: Phase 2 Trial of Brigatinib after Treatment with Next-Generation ALK inhibitors in Refractory ALK Rearranged NSCLC

A description of this clinical trial will be available on http://www.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.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Thomas Stinchcombe at (919) 681-6509 during regular business hours and at (919) 970-2829 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____		
Printed Signature of Subject		
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time
_____		
Printed Signature of Person Obtaining Consent		