Duke University Health System

Consent to Participate in a Research Study
ADULT
Single arm phase 2 trial of atezolizumab and bevacizumab in Epidermal Growth Factor Receptor (EGFR) mutant non-small cell lung cancer in patients with progressive disease after receiving osimertinib (TOP 1901)
PI: Thomas Stinchcombe

CONCISE SUMMARY
This is a research study to find out the safety and efficacy of giving atezolizumab in combination with bevacizumab in patients with EGFR-mutant NSCLC whose cancer has gotten worse while receiving osimertinib.

You will be asked to return every 21 days to receive the study drugs intravenously (IV) and for regularly scheduled check-ups and lab assessments. Blood samples and possibly a small piece of tissue may be collected to determine what type of cancer cells you have. You will also have other tests, exams, and procedures for study purposes and your standard of care. You will be in this research study from the time of your first dose of the study drugs, until your condition worsens, or you experience intolerable side effects as deemed by the study doctor.

There are risks to this study that are described in this document. Some risks include diarrhea, itching, rash, and a feeling of weakness. 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 lung cancer (a type called non-small cell lung cancer or NSCLC) and your cancer has gotten worse while receiving treatment with osimertinib. 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 Genentech and Roche. Genentech and Roche will pay Duke University to perform this research, and these funds may reimburse part of Dr. Stinchcombe's salary. Genentech is supplying the study drug atezolizumab and Roche is supplying the study drug bevacizumab.

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WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Thomas Stinchcombe or a member of his study team 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.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to investigate the safety and efficacy of giving atezolizumab combined with bevacizumab in patients with epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC) whose cancer has gotten worse while receiving osimertinib. The use of atezolizumab combined with bevacizumab in this study is considered investigational. The word "investigational" means the study drugs are still being tested in research studies and are not approved by the U.S. Food and Drug Administration (FDA).

Atezolizumab is an antibody which is a protein to fight foreign tissue including tumor cells. This particular antibody affects your immune system by blocking the activity of PD-L1. The PD-L1 is involved in regulating your body's natural immune response, but tumors can disrupt this pathway and partially resist or evade the immune system by producing excessive amounts of PD-L1. Atezolizumab may help your immune system stop or reverse the growth of tumors by blocking the PD-L1.

Bevacizumab is a monoclonal antibody that blocks the formation of blood vessels that cancer cells need to grow.

In this study, atezolizumab will be given to you in combination with bevacizumab. It is hoped that when atezolizumab is combined with bevacizumab, the study drugs will have anti-tumor activity in EGFR mutant NSCLC in patients who have experienced disease progression on osimertinib.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 39 people will take part in this research study at Duke.

WHAT IS INVOLVED IN THE STUDY?

- **Screening Visit:** You will have medical tests and procedures done to determine if you are suitable to participate in the study. Whether you can be in the study will depend on the results of your medical history, the judgment of the study doctor, and screening tests, which must be performed within 28 days of the beginning of the study. All the procedures that you will need to undergo are described in the table below. The study doctor and/or study staff will discuss these procedures with you.

Duke University Health System

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- **Treatment Period Visits:** If you meet the requirements to enter the study and agree to participate, you will return to the study site to begin the study. The treatment visits will occur on cycles of 21 days (3 weeks). You will be requested to visit the study site on day 1of all the cycles. The study drugs will be given by an injection into a vein (IV) on day 1 of all the cycles. All the procedures that you will need to undergo are described in the table below. The study doctor and/or study staff will discuss these procedures with you.

- **Post-treatment Period Visits:** When you permanently discontinue study treatment, regardless of whether you are terminating the study early or you have completed the study, you will undergo end of treatment evaluations 28 days after the last dose of study drug or prior to starting any subsequent anticancer therapy, you will return for a Safety Follow-up Visit, and information related to adverse events, the medications that you might be taking, and ongoing cancer treatments will be collected. After the Safety Follow up Visit, you will move into the Follow-up Period and will be contacted by telephone, email, or site visit approximately every 3 months, for up to 2 years, if you have come off the study for disease progression to check for any possible new serious adverse events, record all subsequent anticancer therapies, and to check on your long-term health status.

All the procedures that you will need to undergo during each visit are described in the table below. The study doctor and/or study staff will discuss these procedures with you.

Tests and Procedures	Active Monitoring Phase			
	Screening ≤28 days prior to starting study therapy[5]	Day 1 of each cycle[14]	Re-staging every 3 cycles for 17 cycles (1 year) from cycle 1 day 1 then every 6 cycles until disease progression	End of treatment (EOT) (28 days after the last treatment) [4]
Informed Consent	X			
Inclusion/Exclusion	X			
Demography & Medical History including prior therapies and smoking history	X			

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Tests and Procedures	Active Monitoring Phase			
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Local documentation of EGFR exon 19 deletion or exon 21 L858R and histology	X			
ECOG PS	X	X		X
Physical Exam including weight, blood pressure, temp, P, O2 sat[5]	X	X		X
Adverse event assessment	X	X[9]		X
Prior/concomitant medications	X	X		X
Urine protein creatinine ratio	X	X[12]		
Hematology: CBC/ differential[8]	X	X[8]		X
PT/INR, PTT[6]	X[6]			
Chemistry: SGOT (AST), SGPT (ALT), alk phos, T. bili, creatinine	X	X[7]		X
TSH[10]	X	X[10]		
Tumor measurement [3]	X		X[3]	X
MRI or CT scan of brain[11]	X		X[11]	
Pregnancy test[1]	X[1]	X[1]		
Research Blood sample[2,]		X[2]	X	
Tissue sample (only if a stored tumor sample is available) [13]	X			

Duke University Health System

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1. For women of childbearing potential only. Must be done within 48 hours of the first dose of the study drugs. It will be repeated on day 1 of each cycle.
2. Blood sample for research will be drawn at 3 time points: *baseline (cycle 1 day 1), at time of first imaging (9 weeks), and at time of disease progression on study therapy*
3. You will undergo CT imaging with chest and abdomen scans to check for disease progression every 3 cycles for the initial 17 cycles (1 year), and then every 6 cycles until disease progression is found. Tumor measurements should be done 28 days or less prior to starting study drugs. If you discontinue the study drugs prior to disease progression, the study would like to follow you with imaging scans until disease progression is found. The schedule of follow-up imaging is at the discretion of your physician, but may be done at an interval of 6 to 12 weeks.
4. All patients (including those who have left the study because of progressive disease, unacceptable toxicity, patient refusal, investigator's decision to remove patient, etc.) should have an end of treatment visit. However, if it is not feasible due to decline in health, if you have initiated another therapy, or you are being treated at another the end of treatment visit need not occur. This study visit can occur +/- 3 days due to patient convenience and travel.
5. Baseline/screening assessments are to be performed ≤ 28 days prior to starting study therapy unless otherwise specified
6. PT (prothrombin time)/INR (international normalized ratio), PTT (partial thromboplastin time), required at baseline and then only as clinically indicated, discretion of the investigator, or institutional practice. PT/INR and PTT are blood tests to detect a bleeding disorder or excessive clotting disorder.
7. Blood tests to measure only AST (aspartate aminotransferase, aka SGOT [serum glutamic-oxaloacetic transaminase]), ALT (alanine aminotransferase, aka SGPT [serum glutamic-pyruvic transaminase]), alk phos (alkaline phosphatase), T. bili (bilirubin test), and creatinine will be done on Day 1 of each cycle for first 4 cycles, and then every other cycle to measure liver function. More intensive monitoring per investigator discretion.
8. A blood test to measure blood cell counts called a CBC (complete blood count) is required at baseline then day 1 of cycles 1-4, then every other cycle and as clinically indicated, at the discretion of the investigator. CBC is a blood test to check your overall health
9. Prior to subsequent cycle.
10. A blood test to measure TSH (thyroid-stimulating hormone) should be done every 9 weeks. Additional testing may be done at the discretion of the investigator. TSH will test your thyroid gland hormone function.
11. MRI is the preferred test for imaging for brain metastases, but CT scan with contrast is acceptable for patients who are unable or intolerant of undergoing MRI of the brain. Patients must have either MRI or CT scan prior to starting study therapy. MRI and CT scans should be done less than 28 days prior to start of study drugs. Patients with untreated brain metastases

Duke University Health System

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should undergo repeat imaging every 12 weeks or sooner if clinically indicated to assess disease status. Patients without brain metastases or treated brain metastases can undergo repeat imaging at the discretion of the investigator or per institutional practice

12. Urine protein/creatinine ratio should be checked on every 3 cycle
13. Tumor tissue (if available). Archival tissue will be used and analyzed only if a stored (archival) tumor sample was obtained within 60 days of disease progression on osimertinib and prior to Day 1 of study therapy. If a tumor sample is not available, you can still enroll in this research study.
14. The study visits can occur +/- 3 days to accommodate holidays, travel schedule, family events, etc. as necessary

END OF STUDY VISIT

1. A review of interval medical history since the last visit and assessment of performance status (quality of life)
2. A directed physical examination will be performed at the visit with vital signs including pulse, blood pressure, temperature, oxygen saturation, weight
3. Laboratory: chemistry and hematology

FOLLOW-UP PERIOD

After discontinuing study therapy, you will be followed for overall survival every 3 months by telephone or review of medical records until death or a maximum of 2 years from completion of study therapy. Subsequent therapy and survival status will be documented. If molecular testing performed (e.g. molecular testing of tumor biopsy or circulating tumor DNA) as part of standard of care the results of the testing will be recorded if available. Patients who discontinue therapy for reasons other than disease progression will be followed for disease progression. The imaging schedule is at the discretion of the treating physician, but the recommended interval is every 6 to 12 weeks.

HOW LONG WILL I BE IN THIS STUDY?

The duration will vary depending on how you are tolerating the study drugs. Patients will stay on the study as long as they are tolerating the study drugs.

Once you complete these phases of the study, you will enter the Follow-Up phase of the study for approximately 2 years. (We will contact you approximately every 3 months.)

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.

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WHAT ARE THE RISKS OF THE STUDY?

As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider, if you choose.

During the study, the study drugs may cause you to experience discomforts and risks (side effects). Common side effects are listed below, but there may be others that we cannot predict. Your study doctor and your study team will be watching you carefully for side effects. The side effects may vary from person to person. You may experience some, none or all of these side effects and they may be mild to severe and, in some cases, life-threatening. It is also possible that you may experience side effects that have not been seen previously in clinical studies. Your study doctor may order other medications to treat side effects and to make you feel more comfortable. For more information about risks and side effects, please ask your study doctor.

Atezolizumab may cause some, all or none of the side effects listed below.

This information is based on information collected from subjects in other clinical trials with atezolizumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse about any side effects you experience.

Very common side effects of atezolizumab include: (More than 1 out of 10 people [10%]):

- Tiredness
- Infection

Common side effects of atezolizumab include: (More than 1 out of 100 people [1%] to less than 1 out of 10 people [10%])

- Anemia which may require blood transfusion
- Diarrhea, nausea, vomiting
- Difficulty swallowing
- Fever
- Flu-like symptoms including body aches
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Loss of appetite
- Pain in back
- Cough, shortness of breath, stuffy nose

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- Itching, acne, rash

Atezolizumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Pain in belly
- Pain or swelling of the joints
- Rash that develops on skin, nails, scalp and inside of mouth or vagina that may be painful

Uncommon side effects of atezolizumab include: (More than 1 out of 1,000 people [0.1%] to less than 1 out of 100 [1%])

- Bruising, bleeding

Atezolizumab (MPDL3280A) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body
- A condition with high blood sugar which leads to tiredness, frequent urination or excessive thirst
- Swelling and redness of the eye
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling

Duke University Health System

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- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: blisters on the skin

Bevacizumab may cause some, all or none of the side-effects listed below.

Very common side effects of bevacizumab include: (More than 1 out of 10 people [10%]):

- High bold pressure which may cause headaches, dizziness, blurred vision

Common side effects of bevacizumab include: (More than 1 out of 100 people [1%] to Less than 1 out of 10 people [10%])

- Anemia which may require blood transfusion
- Low white cell count that may increase the risk of infection
- Infection, including collection of pus in the belly or rectum
- Abnormal heartbeat which may cause palpitations or fainting
- Pain in the belly, rectum, chest, joints, muscles, or tumor
- Low appetite, constipation, diarrhea, heartburn, nausea, vomiting, or dehydration
- Internal bleeding which may cause black tarry stool, blood in vomit, coughing up of blood, or blood in urine
- Bleeding from other sites, including the vagina or nose
- Blockage of internal organs which may cause vomiting or inability to pass stool
- Sores in mouth
- Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Delay in healing of wounds or spontaneous opening of wounds
- Weight loss, tiredness, or dizziness
- Muscle weakness
- Damage to organs which may cause loss of teeth
- Headache
- Numbness, tingling, or pain in the fingers or toes
- Hoarseness, stuffy nose, or cough
- Dry skin
- Swelling and redness of the skin
- Blood clot in limbs or lungs which may cause swelling, pain, or shortness of breath
- Leakage of protein in the urine, which can rarely lead to damage to the kidney

Duke University Health System

Consent to Participate in a Research Study
ADULT
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PI: Thomas Stinchcombe

Uncommon side effects of bevacizumab include: (More than 1 out of 1,000 people [0.1%] to less than 1 out of 100 people [1%])

- Clots in the arteries, causing stroke (which may cause paralysis or weakness) or heart attack (which may cause chest pain or shortness of breath). This risk is significantly increased in patients who are elderly or with history of diabetes.
- Heart failure which may cause shortness of breath, swelling of ankles, or tiredness
- Bowel perforation (a tear in the bowel) that can cause pain or bleeding and require surgery to repair
- A tear or hole (fistula) in internal organs such as the nose, throat, lungs, esophagus, rectum, or vagina. These conditions may cause serious infections or bleeding and require surgery to repair
- Sores in the throat
- Flesh-eating bacteria syndrome, an infection in the deep layers of skin
- Damage to organs (bone, lungs, others) which may cause loss of function
- Bleeding in the tumor, brain, belly, or lungs which may cause confusion, blood in stool or coughing up blood
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Kidney damage which may require dialysis
- Redness, pain or peeling of palms and soles

For Those of Reproductive Potential:

Reproductive Risks
For women: In animal studies, atezolizumab is associated with an increased risk of pregnancy complications, including miscarriage and stillbirth. Whether these complications affect a developing pregnancy or breastfeeding infant in humans is not known. Women who are pregnant, planning a pregnancy, or breastfeeding are not allowed to participate in studies of the drug.

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 will be performed, and it must be negative in order to continue in the 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. You will also have urine pregnancy tests at follow-up visits as described above, and these also must be negative.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for 7 months after the last dose of study drugs, or one of the following methods of

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contraception: (a) partner vasectomy, (b) bilateral tubal ligation, (c) intrauterine device (IUD), (d) hormonal implants, or (e) condoms and spermicide PLUS a progestin-only birth control pill or injection. Hormonal methods that contain estrogen may increase the risk of blood clots and are not considered safe in women taking other drugs that may also increase those risks. If you are not currently using one of these methods, or if you are using a method which is not considered safe when used with the study drugs, Dr. Stinchcombe will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required by this study.

Because no method of birth control is 100% effective, you should notify the study team immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test. If pregnancy is confirmed, the study drug(s) will be stopped, but Dr. Stinchcombe will continue to follow you to collect information on your health during the pregnancy, and, if appropriate, the health of the baby.

For men: The effects of the study drugs on developing pregnancies that began while the father was taking the drugs are not known. 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) and you have not had a vasectomy, you must agree to either abstain completely from vaginal intercourse for the duration of the study and for 7 months after the last dose of study drug, or use a condom with spermicide for the same length of time. This is true even if your partner is using another method of birth control. You should inform your partner about your participation in this study and the potential risks to a pregnancy. If she is not using another method of birth control, she should discuss options with her doctor. If she does become pregnant during the study, you should inform the study doctor immediately. He will ask her permission to collect information on her health during the pregnancy and, if appropriate, the health of the baby.

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:
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.

Duke University Health System

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ADULT
Single arm phase 2 trial of atezolizumab and bevacizumab in Epidermal Growth Factor Receptor (EGFR) mutant non-small cell lung cancer in patients with progressive disease after receiving osimertinib (TOP 1901)
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Radiation Risks:
You will 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 due to participating in the research. However, if you have concerns about the total radiation exposure you will get, you should discuss them with your physician. The PET, CT or MRI scans are being done as part of your routine medical care for cancer and will be done whether you choose to participate in this study or not.

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

Computed tomography (CT) scan, PET scan: These are radiology procedures which use X-rays (CT) to create pictures of the inside of your body. PET scan is a type of imaging test that uses a radioactive substance called a tracer to look for disease in the body. These pictures will allow your doctor to monitor your disease before, during, and after you receive your study drug and to see if the tumors change in size. A brain CT (or MRI) will also be required to check for any areas of disease in your brain.

MRI: Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. 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. Therefore, we will carefully ask you about metal within your body including medical implants, devices such as pacemakers and internal defibrillators, or certain dyes found in in tattoos. We will also keep the MR room locked so that no one carrying metal objects enters the room while you are in the scanner.

If there is any question about potentially hazardous metal within the body, you will not undergo the MRI. This may exclude you from participation in this research study. The MRI involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire. Let the study doctor know if you have a fear of enclosed spaces.

A rare but serious adverse reaction has been observed in patients that received a gadolinium-based contrast material during MRI examinations, a reaction called nephrogenic systemic fibrosis (NSF). Patients with kidney disease are at increased risk of developing NSF. NSF may cause skin thickening, joint pain and/or swelling. In rare cases, NSF can lead to lung and heart problems and cause death. To

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minimize the likelihood that you will be affected, you will have a blood test to measure your kidney function. If your blood test is abnormal, you will not be permitted to receive gadolinium.

Radiation Exposure Risks:

If you take part in this research, you will have one or more medical imaging studies which use radiation. For this study, a type of scan called an FDG PET (fluorodeoxyglucose-positron emission tomography) CT scan will be done. This involves injection into a vein of a radioactive tracer liquid inside the body that collects at tumors and other sites where cells divide more quickly than usual. About an hour after the injection, you will undergo the scan as described.

The radiation dose from an FDG PET CT scan is about 20 millisievert. To give you an idea about how much radiation you will get, we will make a comparison with an every-day situation. Everyone receives a small amount of unavoidable radiation each year. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. This research gives your body the equivalent of about 7 extra years' worth of this natural radiation. The radiation dose we have discussed is what you will receive from this study only, and does not include any exposure you may have received or will receive from other tests.

A possible health problem seen with radiation exposure is the development of a second 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 is low. 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.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be direct medical benefit to you. This approach has not been tested in people with lung cancer before and it is not known if there will be any benefit. There is the possibility the study drugs, atezolizumab and bevacizumab, may delay the growth of your cancer. However, no benefit to you can be guaranteed. We hope that in the future the information learned from this study will benefit other people with your condition.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
You do not have to participate in this study to be treated for your cancer. You may receive standard chemotherapy or surgery without being in this study. Other investigational studies with chemotherapy, hormones, radiation therapy, or new anticancer drugs may be available for your disease. Your study doctor is very willing to discuss the benefits, risks, and side effects of alternative treatments including the option of treating your symptoms only, with no further cancer therapy. If you decide that you don't

Duke University Health System

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want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

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 Genentech or Roche and their 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 Genentech or Roche, the Duke University Health System Institutional Review Board, the Duke 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. If serious adverse events arise, that data will be collected and reported to Genentech and Roche. 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.

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 (PI-Duke Cancer Institute) of this study. If disclosed by the sponsor, the information is no longer covered by 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 federal privacy regulations.

Duke University Health System

Consent to Participate in a Research Study
ADULT
Single arm phase 2 trial of atezolizumab and bevacizumab in Epidermal Growth Factor Receptor (EGFR) mutant non-small cell lung cancer in patients with progressive disease after receiving osimertinib (TOP 1901)
PI: Thomas Stinchcombe

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.

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.

Genentech and Roche has agreed to support Duke for services and procedures that are done solely for research purposes and that have been reviewed and captured in the contract between Duke and Genentech and Roche. Please talk with the Dr. Stinchcombe and/or the study team about the specific services and procedures (including the device, if applicable) that will be covered by Duke 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 or she can help find a resolution.

Genentech will provide the study drug, atezolizumab, and Roche will provide the study drug bevacizumab free of charge to you. 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.

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WHAT ABOUT COMPENSATION?
You will not be paid to take part in this research study. Your expenses for parking may be reimbursed.

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., Genentech/Roche, or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Thomas Stinchcombe at (919) 681-9509 during regular business hours and at (919) 970-2829 after hours and on weekends and holidays.

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.

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. 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:

Thomas Stinchcombe, MD
Box 3198
Duke University Medical Center
Durham, North Carolina 27710

Dr. Stinchcombe or your study doctor may also 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.

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Genentech, Roche or regulatory agencies may stop this study at any time without your consent. If this occurs, you will be notified and your study doctor will discuss other options with you.

For withdrawal of tumor tissue samples: Your coded tissue samples will be stored in a secure location, at Duke (in MSRB1) with all having alarm systems with on- and off-site monitoring for up to 15 years after the end of the study. 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 on the preceding page.

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) 681-9509 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.

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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."

_____
Printed Name of Subject

_____ _____ _____
Signature of Subject Date Time

_____
Printed Name of Person Obtaining Consent

_____ _____ _____
Signature of Person Obtaining Consent Date Time