INSTITUTE: National Cancer Institute

STUDY NUMBER: 16-C-0092 PRINCIPAL INVESTIGATOR: Udayan Guha, M.D., Ph.D.

STUDY TITLE: A Pilot Study of Local Ablative Therapy for Treatment of Oligoprogressive, EGFR-Mutated, Non-Small Cell Lung Cancer (NSCLC) After Treatment with Osimertinib (AZD9291, Tagrisso)

Continuing Review Approved by the IRB on 01/28/19
Amendment Approved by the IRB on 06/28/19 (L) Date posted to web: 07/04/19
Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

This study is being done in order to test the effect of local ablative therapy (LAT) in the treatment of your cancer after progression of disease on the investigational drug, osimertinib (AZD9291, Tagrisso), provided there are no more than 5 sites of your disease suitable for treatment with LAT (surgery, radiation therapy, radiofrequency ablation, or cryoablation).

Normally, cells in your body divide in an orderly way. However, in cancer, some cells start to behave abnormally resulting in faster growth and multiplication. Osimertinib is an experimental treatment for patients with non-small cell lung cancer (NSCLC) whose lung cancer is due to the development of specific changes in the gene that produces a protein on the surface of the cell called the epidermal growth factor receptor (EGFR). When the gene changes it is said to have developed a mutation. Patients who have NSCLC with a mutation in EGFR can be treated by specific drugs called EGFR tyrosine kinase inhibitors (EGFR TKIs). Unfortunately, after a period of therapy with EGFR TKIs, a significant number of tumours will develop resistance to this treatment due to a second EGFR mutation called T790M.

Osimertinib has been approved by the Food and Drug Administration (FDA) for treatment of recurrent lung cancer with T790M mutation in EGFR after progression on drugs targeting other "sensitizing" mutations in EGFR and has been shown to delay cancer progression. However, osimertinib is not approved for use as the initial treatment of lung cancer with EGFR mutations, treatment of patients without the T790M mutation, or re-initiation of treatment after LAT. Hence treatment with osimertinib is experimental in this study.

There are only two FDA-approved treatments for patients whose disease has progressed on osimertinib (Nivolumab/Opdivo and Pembrolizumab/Keytruda). Thus, assessing the effectiveness of LAT as a strategy to extend the benefits of osimertinib merits further investigation.

Why are you being asked to take part in this study?

You have been asked to take part in this study because you have been diagnosed with non-small cell lung cancer that has an EGFR mutation, with any of the following characteristics:

- You have not been treated with any EGFR TKI. (cohort 1)
- Your lung cancer has progressed after treatment with other EGFR TKIs and now it has the EGFR T790M mutation. (cohort 2)
- Your lung cancer has progressed while being treated with osimertinib and there are no more than 5 sites of your disease that have progressed and are suitable for treatment with LAT (surgery, radiation therapy or radiofrequency ablation). (cohort 3)

How many people will take part in this study?

Up to 100 people will take part in this study.

Description of Research Study

What will happen if you take part in this research study?

Before you begin the study

All research studies have specific criteria for entry to allow for valid interpretation of the study results and safety of participants, known as eligibility criteria. Before you begin this study, you will need to have the following exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care and may be done even if you do not join the study. You may have already had these tests done as part of a NCI protocol, including the screening protocol. If you have recently undergone some of these tests, they may not need to be repeated.

- History and physical examination, including obtaining information about how you function in your daily activities
- Standard blood tests to measure your liver and kidney function, white blood cells, red blood cells and platelets, blood electrolytes and how quickly you form blood clots. If you are a woman able to get pregnant, you will also have a pregnancy test done. You will not be able to participate in the study if you are pregnant.
- Scans of your tumor
- Eye exam
- Electrocardiogram (ECG)
- Echocardiogram
- Review of your tumor sample from previous surgery or biopsy to confirm diagnosis and for genetic testing. If sufficient material does not exist, you will be asked to undergo a biopsy.

If you meet the eligibility criteria for this study you will be offered the option of participating and you will be asked to sign this informed consent document before participating in the study.

During the study

<u>Cohorts 1 and 2</u>

Once you have signed the consent, you will begin taking osimertinib by mouth once a day, on every day of a 28-day course. You will continue to take osimertinib until you have intolerable side effects or if your disease worsens. If your disease worsens, you will be assessed for your suitability for LAT. If you have no more than 5 disease sites that can be treated with LAT, you will undergo the most appropriate procedure (surgery, RFA, or radiation therapy). If your disease is not suitable for LAT, you will be permanently removed from study treatment.

Cohort 3

If you enrolled in the study having already progressed on osimertinib, you will be asked to undergo a biopsy, will be evaluated for eligibility for LAT and if you are eligible, you will undergo the most appropriate LAT procedure before re-starting osimertinib.

All Cohorts

After LAT, you start osimertinib again, taking it daily by mouth until your disease worsens or you have intolerable side effects. If your disease worsens at the same site where you had an LAT procedure done before, you will be considered for further LAT procedure at that site and have an option to be re-started on osimertinib after the 2nd LAT procedure at the same site.

Osimertinib can be taken with or without food at the same time each day. If a dose of osimertinib is missed, you may make up the dose unless the next dose is due within 12 hours. The tablet should be swallowed whole with water. The tablet should not be crushed, split or chewed. If you are unable to swallow the tablet, it may first be dispensed in 50 mL of non-carbonated water. The tablet should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed.

You will be asked to keep a medication diary to record your doses. Please bring the diary and your remaining tablets with you at every study visit.

Study tests/procedures

We will also collect several samples and perform several tests during the study. Some will be to monitor your safety and the progress of your disease. Some will be for additional research studies we plan to conduct.

Clinical Assessments

You will have a physical examination, an ECG, and routine blood tests on day -1 and day 7 of your first course, then on day -1 of all subsequent courses.

Scans to assess the response of your disease to the study therapy will be performed every 8 weeks.

An echocardiogram will be performed every four months.

Research Assessments

The following samples will be collected at baseline (before you have had your first dose of study drug) and day 7 of course 1 and on day -1 of subsequent courses:

- **Blood sample:** We will ask you to provide up to 50mL (approximately 3.5 tablespoons) of blood at the above time points. The maximum amount of blood taken from you is based on your age and will not be more than the blood volume limit set for research by the NIH.

- **Urine sample:** We will ask you to provide up to 45 mL of urine at each sampling time point, if feasible. We may also provide you with a container to collect urine for a 24hr period at home, or during your stay in the NIH Clinical Center.
- **Saliva sample:** We will ask you to provide a saliva sample, if possible, each time you provide us with your blood and urine samples. We will provide you with a container with specific instructions to get your saliva samples.

The above samples will be analyzed for alterations in genes and proteins.

We will also collect tumor tissue at the beginning of the study before you have taken any study medication (if we have enough tissue left from your sample at screening, we will use that), and after your disease worsens for the first time. We may also collect a sample after your disease has worsened for the second time, but this is optional, and we will ask your permission to do so later on in the consent.

If you undergo surgery as your form of LAT, the tumor sample will be obtained at that time. If you are not undergoing surgery at the time the sample is needed, you will have to undergo a biopsy, a description of which is provided later.

When you are finished taking the drugs (treatment)

Approximately 30 days after you have finished taking the study drug, you will be asked to the return to the NIH for a medical history and physical exam, an ECG, routine blood tests for safety.

After you are no longer coming to the Clinical Center for visits, we will contact you by phone every year to check on your health.

Standard of Care Treatment:

Treatments covered under this study may include a single medication or a combination of medications, surgery or radiation to treat your cancer. These treatments will not be experimental. Your doctors will describe your treatment plan to you in detail before asking you to sign this

consent form. You may be asked to sign a separate consent form for any treatment procedures not outlined in this consent.

Birth Control

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Acceptable forms of birth control for women include:

- abstinence
- intrauterine device (IUD)
- hormonal [injections or implants].

  Note: use oral hormonal contraception alone is not recommended as the study medication may reduce its effectiveness.

- tubal ligation
- vasectomy

Acceptable forms of birth control for men:

- condoms (should be used even if your female partner is on another form of contraception)

You should also refrain from donating sperm for 6 months after your last dose

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

Risks from osimertinib

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

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

Here are important points about side effects:

- The study doctors do not know if you will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

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

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

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

Likely	**Less Likely**	**Rare but Serious**
• Nausea • Diarrhea • Rash, Acne • Dry Skin, Itching • Infection of the skin around a fingernail or toenail • Eye Discomfort: burning / itching / irritation / smarting/ redness with or without discharge • Blurred vision • Light sensitivity	• Pneumonia • Pneumonitis, an inflammation of lung tissue • Pleural Effusion, a condition of excess fluid in the pleural cavity, the fluid-filled space that surrounds the lungs • Interstitial Lung Disease (ILD), a variety of conditions characterized by the scarring of lung tissue • Heart function: changes in how well your heart pumps with each beat • Change in heart rhythm • Increased levels of calcium in the blood • Vision Changes	• Septic Shock, a severe infection where toxins can cause a full-body inflammatory response • Death

The risks you might experience other than the drug side effects are:

Biopsies

Risks associated with the biopsies include pain and bleeding at the biopsy site. We may need to perform a CT scan to guide the collection of tissue which would involve risks from radiation as described below.

Radiation risks: You will be asked to undergo CT-guided biopsy before initiating treatment even if you had undergone a biopsy before. In case a biopsy at this time is not clinically safe and you had a biopsy done before, tissue will be obtained from the previous biopsy for the mutation testing needed for your eligibility for this protocol. A 2nd biopsy is also required after your first progression on osimertinib to detect the T790M mutation in EGFR to guide your therapy and also for research purposes. Another optional CT-guided biopsy may be requested when you finally come off protocol because of disease progression. One or more of these CT-guided biopsies may be for research purposes only and may or may not affect your future treatment. Therefore, the study may involve exposure to radiation from up to 3 CT scans. This radiation exposure is not required for your medical care and is for research purposes only.

The amount of radiation you will receive in this study is 2.4 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of radiation exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant you will not be permitted to participate in this research study. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

Blood draw

Risks associated with blood draw, which include pain and bruising, lightheadedness, and rarely, fainting

Privacy

Psychological or Social Risks Associated with Loss of Privacy in Genetic Research

1. Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

   As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

   Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress.

2. Privacy Risks Associated with Return of Incidental or Secondary Findings

   Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all of the safety measures that we will use, we cannot guarantee that your identity will never become known. While neither the public nor the controlled-access databases developed for this project will have information such as your name, address, telephone number, or social security number, it may be possible to identify you based on the information in these databases and other public information (including information you tell people or post about yourself). The risk of this happening is currently very low.

   Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives.

   It is possible also that someone could get unauthorized access or break into the system that stores information about you. Every precaution will be taken to minimize this risk. There also may be other privacy risks that we have not foreseen.

3. Protections against misuse of genetic information

   Since some genetic variations can help to predict future health problems for you and your relatives, this information might be of interest to health care providers, life insurance companies, and others. However, Federal and State laws provide some protections against discrimination based on genetic information. For example, the Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, GINA does not prevent companies that sell life insurance, disability insurance, or long-term care insurance from using genetic information as a reason to deny coverage or set premiums. GINA also does not apply to members of the United States military, individuals

covered by the Indian Health Service, or veterans obtaining health care through the Veteran's Administration. Lastly, GINA does not forbid insurance medical underwriting based on your current health status though the Affordable Care Act limits consideration of pre-existing conditions by insurers.

Risks of local ablative therapy (LAT)

You will be required to sign separate consent forms at the time of LAT. Surgery, radiation therapy, or radiofrequency ablation have their own risks and these will be explained to you if and when you are eligible for that. You have the option of declining the LAT part of the study at that time. Prior osimertinib treatment may have unknown risks associated with subsequent LAT procedure, including radiation.

Incidental findings

Your tissue (tumor and normal tissue) and blood that is collected will be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) are the molecules inside cells that carry genetic information and pass it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow. In order to determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze all of the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. In order to examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), growing your tissue for a short time in culture in the laboratory and growing your tumor tissue in mouse models and looking in great detail at the parts of the genes that produce specific proteins. When we are examining these pieces of your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings". These include:

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

However, the analyses that we will perform in our laboratory are for research purposes only. They are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the results of testing on your tissue and blood

that is performed in our research lab. However, in the unlikely event that we discover a finding that could be clinically relevant, we will contact you to ask if you would like to submit a blood sample to be tested at a certified lab and meet with a credentialed genetics healthcare provider for genetics education and counseling (either in clinic or via phone conference). The genetics healthcare provider will explain to you the nature of the result, implications for you and your family members, the need to confirm the results with an outside certified laboratory, the time frame for analysis, and implications of results including risks, benefits, and limitations.

At the start of the study, we will give you the option to complete a form to name a person (a designee) that you would like to receive information about your genetic findings. If we find a change in a gene that is important to you or your family's health, but you are deceased or have diminished mental capacity at the time results are available, we will offer your designee to come to NIH (at our expense) to have genetic education and counseling to explain this result. If your designee does not want to come to NIH, we will help the designee find a local genetic healthcare provider who can explain the result (at the designee's expense).

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to see if LAT and re-initiation of treatment with osimertinib can increase the time before your disease gets worse. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about this strategy of LAT and re-initiation of osimertinib, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Alternative Approaches or Treatments

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

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

Stopping Therapy

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back after LAT or if you are not eligible for LAT
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if AstraZeneca is no longer able to supply osimertinib

In this case, you will be informed of the reason therapy is being stopped.

If your doctor decides to stop your therapy because your disease has come back, and that disease is later found to be a non-cancerous diagnosis such as infection or inflammation, you may be able to restart treatment as long as you continue to meet the study's enrollment requirements and have not stopped taking the study drug for more than one month.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the pharmaceutical company or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.

- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.

- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Astra Zeneca, the pharmaceutical company who produces osimertinib.

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.

Your individual genomic data and health information will be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database have agreed not to attempt to identify you.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or

- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study are using osimertinib developed by Astra Zeneca through a joint study with your researchers and the company. The company also provides financial support for this study.

Biopsy Procedure

A mandatory tumor biopsy will be obtained before starting treatment and after first progression. You will be asked about another tumor biopsy at second progression. This biopsy will be optional.

If your doctor determines it is safe we will obtain a piece of your tumor (biopsy) using a needle. This process will be guided by a CT scan or bronchoscopy and is minimally invasive. You will be given local anesthesia (numbing medicine). The biopsy will be taken through a needle put through the skin into your tumor. After the procedure the nurses will watch your blood pressure and other vital signs.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Udayan Guha, M.D., Building 10, Room 4-5330, Telephone: 240-760-6241. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative — Date

Print Name

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.

(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian — Date

Print Name

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian — Date — Print Name

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JANUARY 28, 2019 THROUGH FEBRUARY 4, 2020.

Signature of Investigator — Date

Print Name

Signature of Witness — Date

Print Name