PRINCIPAL INVESTIGATOR: **Arun Rajan, MD**

STUDY TITLE: **Pilot Trial of Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and Thymic Malignancies**

STUDY SITE: **NIH Clinical Center**

Cohort: Family Member

Consent Version: 12/04/2019

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Arun Rajan, MD
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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Your blood and tissue samples contain genes, which are made up of DNA (deoxyribonucleic acid) which serves as the "instruction book" for the cells that make up our bodies. We are conducting a study to see if it is possible to analyze the genes of patients with lung cancer and cancers of the thymus and based on such analysis provide personalized treatment with drugs that target the specific gene abnormalities (mutations) found in the tumor.

As part of this study, we are also studying specific hereditary mutations (those mutations which can be passed from one generation to the next) and their possible role in the risk of developing lung cancer. Genetic testing for hereditary mutations is part of the care of individuals who have a family history of other types of cancers, such as breast, ovarian, or colon cancer. However, little is known about hereditary mutations that may be a factor in the development of lung cancer.

We are specifically interested in the epidermal growth factor receptor (EGFR) gene. Non-hereditary mutations (those mutations found in the tumor and not passed from one generation to another) in this gene are known to be present in the tumor of some individuals with lung cancer and may have implications in selection of treatment in such patients. Hereditary mutations of EGFR gene have been reported very rarely in the medical literature thus far. From the limited available knowledge on hereditary mutations of EGFR gene, we do not know if having this mutation confers an increased risk of developing lung cancer.

Because one of your first-degree relatives (your parents, siblings, or children) carries a mutation in the EGFR gene, we are requesting your permission to test your blood for the same mutation.

By studying the pattern of these mutations in patients with lung cancer and their family members, we hope to gain a better understanding of the role of hereditary EGFR gene mutations in the development of lung cancer. If testing reveals a hereditary mutation in your EGFR gene, we would also like to invite your adult first-degree relatives (your parents, siblings, and children) to participate in the study and undergo genetic testing.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to participate in the study because you are at least 18 years old and one of your first-degree relatives (parents, siblings, or children) has a hereditary mutation of the EGFR gene.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 600 patients with non-small cell lung cancer, small cell lung cancer, cancers of the thymus, a T790M mutation in the absence of cancer, or a family history of lung cancer not related to smoking will take part in the study as a whole. We plan to include 15 families in this part of the study in which we are studying specific hereditary mutations in lung cancer.

DESCRIPTION OF RESEARCH STUDY

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

Before the testing

If you choose to participate in the study, you will need to have the following before the genetic testing:

- Clinic visit, which will include a medical and family history and a physical examination.
- Speak with a genetics health care professional (in person or by phone before the genetic testing is done), who will explain the testing, the types of information that may be learned, the limitations of the testing, and any potential healthcare recommendations that could result. You will be able to ask any questions that you have about the genetic testing.

If you are a smoker, you will be offered help to stop smoking as part of this study.

Testing and results

The genetic testing involves a single blood draw (about 1 teaspoon). It will take about 2 to 3 weeks to get the results. The genetics health care professional will tell you whether or not you carry the mutation, and you will be given a copy of the results in writing.

FOLLOW-UP

Recommendations will be made based on your genetic testing results and your level of risk for developing lung cancer, which is determined by your age, exposure to cigarette smoke, and family history of lung cancer.

If you are found NOT to carry the hereditary EGFR mutation:

- If you are at **high risk** for developing lung cancer, we will recommend that you have screening imaging tests yearly for a certain number of years to check for signs of cancer; these would need to be done through your regular doctor.
- If you are at **low risk** for developing lung cancer, no screening tests will be recommended.

If you are found to carry the hereditary EGFR mutation:

- If testing reveals a hereditary mutation in your EGFR gene, with your permission, we will invite your adult first-degree relatives (parents, siblings, and children who are 18 years of age or older) to participate in the study and undergo genetic testing. We will contact them by a letter followed by phone call.
- If you are at **high risk** for developing lung cancer, we will recommend that you have screening imaging tests immediately and then yearly for a certain number of years to check for signs of cancer; these would need to be done through your regular doctor.
- If you are at **low risk** for developing lung cancer, we will recommend that you have screening imaging tests yearly for a certain number of years to check for signs of cancer; these would need to be done through your regular doctor.

Regardless of your genetic test results and assessed risk, we would like to continue to follow you for your entire life. This is with the intention to learn more about the patterns of lung cancer related to genetic characteristics in families. The follow-up will be a yearly phone call to ask about your health status.

RISKS OR DISCOMFORTS OF PARTICIPATION

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

Physical risks

Risks associated with the blood draw include pain at the needle site, bruising, possible dizziness if you stand up quickly and possible inflammation of the vein or infection at the needle site. Care will be taken to avoid these complications.

Emotional and psychological risks

Genetic information about you and your family may be discovered during this genetic testing. Many aspects of life can be affected by knowing this information. An important thing to consider in deciding whether or not to participate in this type of research is the effect that knowing information about your genetic risks could have on you and others. Not all family members may feel the same about involvement in this research project. Some family members may not wish to participate in the study. Your emotional well being could be affected by information about how your genetic risks could change your health. You might become anxious, depressed or stressed by learning this information. In addition, because this information could have implications for the risks and future health of your children, brothers and sisters and other relatives, it could also affect your relationships with them.

Part of the research may involve testing genetic material from parents and their children. We may learn that a child was adopted or that a child's stated father is not the natural father. Our policy is to not reveal this information unless it has direct medical or reproductive implications for you or your family.

Confidentiality and availability of genetic data

The exact order of the base pairs (chemical letters) in your DNA is known as your DNA sequence. We will be looking at sections of your DNA sequence (in the EGFR gene) and not your entire sequence. Your DNA sequence that is determined as part of the genetic testing will be labeled with a number and not your name. Only medical personnel involved in this study will have access to both your name and DNA sequence. You need to be aware that DNA sequence is like a fingerprint. Theoretically, if enough DNA sequence information is available, someone could identify you based on your DNA sequence if they know some of your DNA sequence already.

Psychological or social risks associated with loss of privacy

- 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. 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.
- While neither the public nor the controlled-access databases developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.

- Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress.
- There also may be other privacy risks that we have not foreseen.

There are state and federal laws that protect against genetic discrimination. There is also a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not apply to members of the United States military, to veterans obtaining health care through the Veteran's Administration or the Indian Health Service. Lastly, GINA does not forbid insurance medical underwriting based on your current health status.

The research team may share your information with:

- The Department of Health and Human Services (HHS), to complete federal responsibilities for audit or evaluation of this project;
- Public health agencies, to complete public health reporting requirements;
- NIH representatives, to complete NIH responsibilities for oversight of this study;
- Your primary care physician if a medical condition that needs urgent attention is discovered;
- Appropriate authorities to the extent necessary to prevent serious harm to yourself or others.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

This research may increase our understanding of genetic risk factors for lung cancer. There may be no direct benefit to you or your family from participating in this research. However, information learned from this study may help your doctor manage your care. We hope that this and related research may contribute to the early diagnosis of lung cancer in the future. Treatment might be more effective when tumors are found early.

ALTERNATIVE APPROACHES OR TREATMENTS

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

You can choose not to participate in the study. The choice to participate is completely up to you. No matter what you decide to do, your decision will not affect the medical care or benefits to which you are otherwise entitled.

STOPPING PARTICIPATION

You can stop taking part in the study at any time. Tell your study doctor if you would like to stop. Your participation could end early if the study is closed for any reason

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.

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.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in

the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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:

1. The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
2. National Institutes of Health Intramural Institutional Review Board

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens and data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

- is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
- is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
- is for other research;
- is disclosed with your consent

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, Arun Rajan, MD, (rajana@mail.nih.gov, 240-760-6236). You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.