ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

PROTOCOL UPDATE FOR ALLIANCE A151216

Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST)
A screening trial for ALCHEMIST treatment trials

[X] **Update:**	[ ] **Status Change:**
[ ] Eligibility changes	[ ] Activation
[ ] Therapy / Dose Modifications / Study Calendar changes	[ ] Closure
[ ] Informed Consent changes	[ ] Suspension / temporary closure
[X] Scientific / Statistical Considerations changes	[ ] Reactivation
[ ] Data Submission / Forms changes	
[X] Editorial / Administrative changes	
[X] Other: Appendices II, III, and IV	

If your site utilizes the CIRB as your IRB of record:
No recommended IRB level of review is provided by the Alliance as the CIRB is the IRB of record for this trial. The site has 30 days after the posting of this amendment to implement it at their site. Please refer to the CIRB amendment application and guidelines for further instructions.

If your site utilizes a local IRB as your IRB of record: Expedited IRB Approval allowed
IRB approval (or disapproval) is required within 90 days. Please follow your local IRB guidelines. The proposed changes in this amendment are minor and do not affect the overall risk/benefit ratio.

UPDATES TO PROTOCOL:

Cover Page

- Sharmila Giri has replaced Shauna Hillman as Secondary Statistician; all contact information has been updated.
- The contact information for the protocol coordinator has been updated.

Schema

The asterisks have been removed from the "Pre-register" and "Register" boxes as these previously referenced a footnote which was removed in a previous protocol update.

Section 7.2 (Baseline Clinical Information), Section 7.7 (Inclusion of Women and Minorities)

"Gender" has been replaced by "sex" throughout these sections per NCI requirement.

Appendix II

Under "Block and Slide Preparation," the first bullet under "Preparation of Tissue Slides" was updated to remove references to 5 10-micron slides, a requirement which was removed in a previous protocol update.

Appendix III

- A sentence has been added to the end of the subsection, "Additional exploratory genomic analyses" to indicate interest in assessing prognostic value of the gene set summaries based on RNA expression data.
- In the "Epidemiologic data" subsection, the last sentence has been edited to indicate that baseline clinical data are transferred on a weekly basis.
- In the "Statistical Considerations" subsection under "Aim 3: Identify genomic features associated with early NSCLC recurrence," a new sentence has been added: "Delayed entry into the study will be handled with left truncation, to account for the fact that DFS time is conditional on having survived (registered) to enter the trial."
- In the "Variables" subsection under "Aim 3: Identify genomic features associated with early NSCLC recurrence," the first sentence has been edited to replace "Gender" with "Sex" per NCI requirement and to add additional detail to the "Receipt of adjuvant chemo" variable.
- In the "Variables" subsection under "Aim 3: Identify genomic features associated with early NSCLC recurrence," the primary genomic features of interest were updated to specify three tiers in order of importance with corresponding references added, as well as secondary genomic features of potential interest.
- The "Model estimation" subsection under "Aim 3: Identify genomic features associated with early NSCLC recurrence" has been updated throughout to add detail about model scores and assessment of Tiers 1, 2, and 3 genomic variables.

Appendix IV: Proteomic Analysis Plan

- Under "Allocation of patients in each Aim," the Figure 1 caption has been updated to remove references to standard of care.
- In the "Variables" subsection under "Final prognostic model estimation analyses (C3 in Figure 1)," detail has been added to the "receipt of all planned adjuvant chemotherapy cycles" variable to indicate "(as a time dependent adjustor variable, will not be included in patient scores)."
- The "Model estimation" subsection under "Final prognostic model estimation analyses (C3 in Figure 1)" has been updated throughout to add detail about penalized time to event regression and delayed entry at registration and model scores.
- In the "Sample size considerations" section, "observation" arm has been replaced by "control" arm.
- New references numbered 7 through 14 have been added; subsequent references have been renumbered accordingly.

UPDATES TO MODEL CONSENT FORM:

There are no changes to the model consent form.

A replacement protocol and model consent document have been issued.

ATTACH TO THE FRONT OF EVERY COPY OF THIS PROTOCOL

Study Title for Study Participants:

Genetic Testing For Patients with Resectable or Resected Lung Cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

Protocol A151216: Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST)

WHAT IS THE USUAL APPROACH TO MY CANCER?

Your lung cancer tumor has either been removed or will be removed by a surgeon. As part of your normal treatment, you may receive chemotherapy or radiation therapy to reduce the chance of the cancer coming back. Today, therapy is not based on tumor genetic testing, but this trial is trying to see if tumor genetic testing would be helpful at guiding treatment in patients such as you. The treatment you will receive, chemotherapy and possibly radiation therapy, is based on current standard therapy that patients with your type of cancer receive.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS SCREENING STUDY?

If you decide not to take part in this study, you have other choices for your care. For example:

- you may choose to have standard therapy without having any tumor genetic testing;
- you may choose to take part in a different research study if one is available
- or you may choose not to receive additional treatment for your cancer at this time

WHY IS THIS SCREENING STUDY BEING DONE?

The purpose of this research study is to examine lung cancer patients' surgically removed tumors for certain genetic changes, and to possibly refer these patients to a treatment study with drugs that may specifically target tumors that have these genetic changes.

Genetic testing will be done to learn if your tumor has any of these genetic changes. These tests will look at the genetic material of the tumor cells. All tissues in the body are made up of cells. Those cells contain DNA, which is your unique genetic material that carries the instructions for your body's development and function. Cancer can develop when changes in certain genes cause those cells to divide in an uncontrolled way and, sometimes, to travel to other organs.

We are interested to see if your tumor tissue might have several different genetic changes. If your tumor is found to have one of these genetic changes you may be invited to participate on a trial that will look at drugs which may target tumors that have these specific genetic

changes. There will be about 8300 people taking part in this screening study by having genetic tests of their tumors.

If you do not go onto one of the treatment trials you are tested for, your doctor will provide you with other options for your care and you will be followed for 5 years. A doctor or research staff will contact you every 6 months for 5 years to determine the status of your cancer and your overall health. This will help doctors better understand what happens to patients receiving the standard treatment for the disease.

Another purpose of this research study is to learn more about cancer and why treatments may be more effective or even stop working with some tumors or in certain patients. After your tumor tissue is screened, if there is any tissue left, the remainder of your coded tissue samples will be sent to a National Cancer Institute (NCI)-sponsored storage facility, currently known as the Biospecimen Core Resource (BCR). The samples will be processed there and portions of your samples then will be sent to different types of laboratories, all within the NCI facility, as part of this project. Additionally, if your cancer comes back and there is biopsy tissue available for analysis, this too will be studied in that way. One type of laboratory will analyze your DNA by a method called sequencing. Other types of laboratories will study other biochemical material from your samples by different methods. All patients will participate in this part of study.

Information from analyses of your samples and your medical information, which may include genetic information, will be put into databases along with information from the other people who volunteered for this project. These databases will be accessible by the Internet in two ways:

- Some of the results from the analysis will be added to the results from other participants and put in a completely public database, available to anyone on the Internet. This information will not be specific to you or any other participant.
- The other database is private, and will include person-by-person coded genetic, biochemical and medical information. The results in this database will be available to the global biomedical research community, but the access is controlled. Only researchers who have received approval from an NIH Data Access Committee will be authorized to access this database.

Your individual results from this research project will not be given back to you or put into your medical records.

If research from this project is published in professional journals, it will not include traditionally-used identifying information, such as your name, address, telephone number, or social security number. Some publications from this project will be found at the www.cancergenome.nih.gov website.

You will be asked later, in the “Optional Study” portion of this consent, to ask if remaining portions of your samples can be stored for possible future use. If you or your doctor requests the return of your samples from the laboratory, every effort will be made to return the samples if there is any remaining.

If your cancer comes back you will be asked to have a biopsy if that is appropriate for your medical care. Generally, tissue is needed by your doctor to determine your diagnosis. If tissue is available it will be sent to researchers to further study the genetic changes in your tumor.

WHAT ARE THE POSSIBLE TREATMENT STUDIES I COULD BE OFFERED BASED ON THE RESULTS OF MY GENETIC TESTS?

Depending on the results of the tissue testing, your physician will help you decide what treatment you will receive. You may not receive treatment on any trial.

If your cancer comes back you will be asked to have a biopsy if that is appropriate for your medical care. Generally, tissue is needed by your doctor to determine your diagnosis. If tissue is available it will be sent to researchers to further study the genetic changes in your tumor. This is because tumors can change during treatment and investigators are interested in seeing what these changes are.

HOW LONG WILL I BE IN THIS SCREENING STUDY?

Patients who go onto one of the treatment studies described in this consent will be followed on that study. If you do not go onto one of the treatment studies a researcher from your hospital will contact you every 6 months for 5 years to check on the status of your cancer and overall general health. Your biopsy may still be used for future research if you consent.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS SCREENING STUDY?

Most of the exams, tests, and procedures you will have are part of the usual care for your cancer.

You will need to have the following extra exams, tests and procedures to find out if you can be in the research study:

- At the beginning of the study the researcher may ask you some extra questions about family and personal history.
- You will have about 2 tablespoons of blood drawn as part of this research study. The blood will be obtained at the beginning of the study to help the researchers study genetic changes. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise. One blood sample will be processed to collect your non-tumor genetic information and will be used to compare to the tumor genetic testing. The other 2 blood samples will be used in the future, to study circulating tumor DNA in the blood. To help you make your decision, additional information is included in the “Risks” section of this consent.
- Tumor tissue collected at the time of your surgery will be sent to a central laboratory for genetic testing.

- You may be offered the opportunity to participate in a treatment trial related to this screening study. Before enrolling on a trial, you will be asked to provide a consent for that specific trial. As part of that process, extra exams or procedures required for that trial will be explained.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS SCREENING STUDY?

If you choose to take part in this research study, there is a risk that:

- 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 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 relative) in another database and be able to identify you (or your 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 may suggest the possibility of future health problems of you and your relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a relative) carry a genetic disease or by leading to the denial of employment or insurance for you (or a relative).
- There also may be other privacy risks that we have not foreseen. Even if you withdraw from this study the data collected and entered into a database will still be available for public viewing.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS SCREENING STUDY?

- This research study may help researchers learn things that may help other people in the future.
- Your study doctor will be given your genetic test results, and those may allow you to enroll in a treatment study.

CAN I STOP BEING IN THE SCREENING STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

If you withdraw, we will stop collecting any of your information and will no longer distribute your samples to anyone – they will be discarded. However, please understand that, even if you do withdraw, once your samples have been distributed to the participating research centers and your information transferred to the databases, it will not be possible to discard your samples or remove your information from this research project.

If you withdraw from this project, it will in no way affect the care you receive from this hospital.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS SCREENING STUDY?

Taking part in this research study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number)*. *(Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

WHAT ARE THE COSTS OF TAKING PART IN THIS SCREENING STUDY?

You or your health plan/insurance company will need to pay for the surgery and collection of the tumor. The screening testing done on the biopsy tumor tissue will be paid for by the National Cancer Institute (NCI) as part of this study. Before you decide to be in the research study, you should check with your health plan or insurance company to find out exactly what they will pay for.

If after treatment your cancer comes back, you will be asked to have a diagnostic biopsy,

unless your doctor determines the biopsy is not appropriate for your medical care. If you choose to have the biopsy, the remaining tumor tissue from your diagnostic biopsy not used for diagnostic purposes will be submitted for research genomics. The research genomics will be paid for by the NCI, but you or your health plan/insurance company will need to pay for the biopsy and collection of the tumor.

You will not be paid for taking part in any part of this research study.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS SCREENING STUDY?

If you are injured or hurt as a result of taking part in this research study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for your injury. Your insurance company may not be willing to pay for research study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to seek recovery for any injuries or damages even though you are in a research study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Alliance;
- The Alliance Data Monitoring Committee, a group of experts who regularly review the progress of the study;
- The local Institutional Review Board (IRB), a group of people at this institution who review the research study to protect your rights;
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA) and the Office for Human Research Protection (OHRP), involved in keeping research safe for people;
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials;
- The National Clinical Trials Network and the groups it works with to conduct research
- Flagship Biosciences, the laboratory doing the genomic testing, will also be getting a copy of your pathology report, which is a report describing the tumor that was

removed.

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS SCREENING STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (insert name of study doctor[s]) at _____ (insert telephone number).

OPTIONAL BANKING STUDY

If there is any leftover tissue and/or blood samples after the completion of the studies described above, the study researchers would like to store the unused tissue and/or blood at the Biospecimen Core Resource (BCR) for possible future use in research related to cancer or, perhaps, in other research projects. Please check the box below to show whether or not you would like to have your tissue and/or blood, along with related clinical and genomic information, stored indefinitely and possibly used for future research:

1) My samples and related information may be kept at the BCR for use in future health research.

____ YES ____ NO

MY SIGNATURE AGREEING TO TAKE PART IN THIS SCREENING STUDY

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the screening study and possibly be referred to a subsequent treatment trial based on the results of my genetic tests.

Participant's signature _____

Date of signature _____

(The following signature and date lines for the person(s) conducting the discussion may be included at the discretion of the study sponsor.)

Signature of person(s) conducting the informed consent discussion _____

Date of signature _____