AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK

ACRIN 4703

Detection of Early lung Cancer Among Military Personnel Study 1 (DECAMP-1): Diagnosis and Surveillance of Indeterminate Pulmonary Nodules

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Limited Site Participation

The Detection of Early lung Cancer Among Military Personnel (DECAMP) consortium is a multidisciplinary and translational research program that includes 7 Veterans Administration Hospitals (VAH), the 4 designated Military Treatment Facilities (MTF) and three academic hospitals as clinical study sites, several molecular biomarker laboratories, along with Biostatics, Bioinformatics, Pathology and Biorepository cores.

The clinical sites will include: Naval Medical Center, Portsmouth, VA; Walter Reed National Military, MD; Naval Medical Center San Diego, CA; San Antonio Military Center, TX; Veterans Administration Boston Healthcare System, MA; Dallas Veterans Administration Medical Center, TX; Denver Veterans Administration Medical Center, CO; Greater LA Veterans Administration Healthcare System, CA; Ronald Reagan University of California, Los Angeles, Medical Center; Veterans Administration Tennessee Valley Healthcare System, TN; Philadelphia Veterans Administration Medical Center, PA; Hospital of the University of Pennsylvania, PA; Veterans Administration Pittsburgh Healthcare System, PA; and Roswell Park Cancer Institute, Buffalo, NY.

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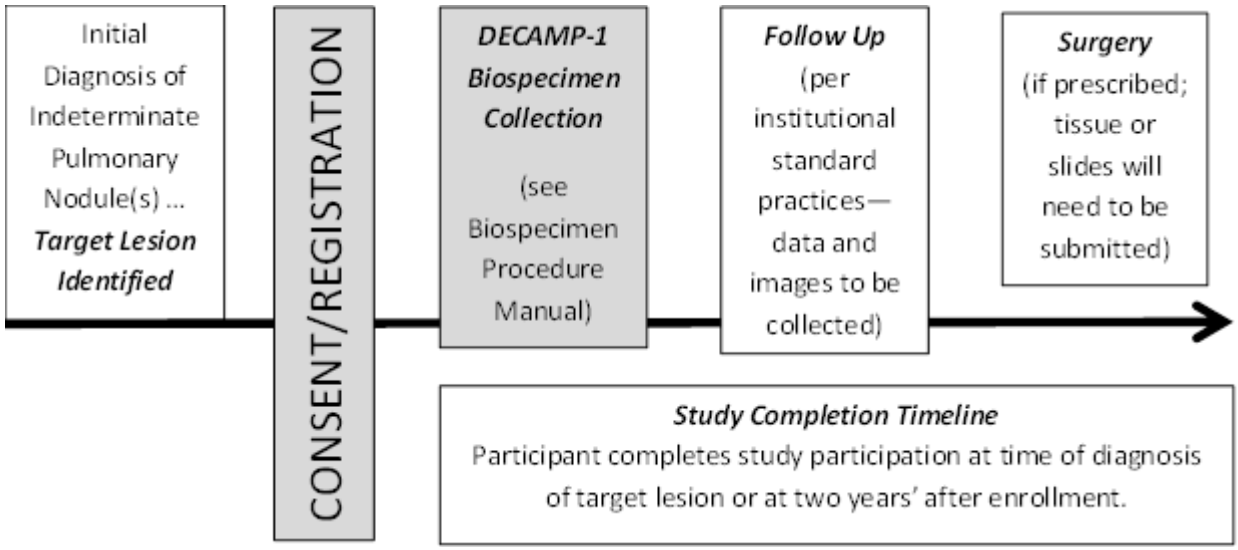
Schema



STUDY OBJECTIVE

The goal of this Phase III project is to improve the efficiency of diagnosing indeterminate pulmonary nodules. Biomarkers for lung cancer diagnosis will be evaluated for their ability to distinguish between malignant vs. benign nodules. Minimally- and non-invasive biospecimens will be collected from military personnel and their families who are at high risk for lung cancer due to smoking history.

ELIGIBILITY (see Section 5.0 for details)

Patients diagnosed with indeterminate pulmonary nodule(s) (target lesion size: 0.7 to 3.0 cm) within 12 months prior to consent (and still of appropriate size at enrollment), ≥ 45 years old, and have a smoking status as a current or former smoker with ≥ 20 pack years (pack years = number of packs per day x number of years smoked).

SAMPLE SIZE 500 eligible participants are projected to participate for this study.

DECAMP-1 and DECAMP-2 are clinical trials developed under Department of Defense (DoD) and funded through the DoD Lung Cancer Research Program.

ABSTRACT

This protocol for human research study is conducted according to United States and international standards of Good Clinical Practice (International Conference on Harmonisation [ICH] Guidelines), applicable government regulations (e.g. Title 45, Part 46 Code of Federal Regulations) and the American College of Radiology Imaging Network (ACRIN) research policies and procedures.

Lung cancer is the leading cause of death from cancer in the United States and the world, with cigarette smoking as its major cause. Lung-cancer associated mortality has remained essentially unchanged over the last 3 decades, in part because of our inability to detect lung cancer at its earliest and potentially curable stage. Military personnel have higher rates of smoking than the general population as well as exposure to other carcinogens, and there is a significantly higher incidence of lung cancer among military veterans. There is therefore an urgent need to develop new approaches for the early detection of lung cancer in this high-risk population. The broad goals of the DECAMP consortium are to develop and validate molecular biomarkers that can serve as tools for the early detection of lung cancer. While the recent National Lung Screening Trial (NLST) demonstrated that screening for lung cancer by low-dose CT leads to a significant reduction of lung cancer specific mortality, biomarkers are needed to 1) determine which of the frequently detected lung nodules on CT scan are malignant and 2) further define the large high-risk population that would be eligible for screening by CT to increase the efficacy of screening and to reduce the cost and morbidity associated with it. This study will investigate a number of airway and blood-based molecular biomarkers that may distinguish benign versus malignant diseases among smokers with indeterminate pulmonary nodules found on CT chest (i.e., in the diagnostic setting). In addition, the DECAMP consortium will establish a unique high-quality clinical, imaging, and biological repository (including bronchial airway brushings and biopsies, nasal and buccal brushings, blood, urine and sputum) from patients at military, Veterans (VA), and academic hospitals across the US. All participating sites will acquire biosamples following the same Standard Operating Procedures (SOPs), and these biosamples will be securely deposited in central biorepositories to support these studies and future correlative studies. The goal is to improve the efficiency of the diagnostic follow up of patients with indeterminate pulmonary nodules. In this Phase III project, the DECAMP consortium intends to determine whether diagnostic biomarkers measured in minimally invasive biospecimens are able to distinguish malignant from benign pulmonary nodules incidentally detected in high-risk smokers on imaging.

BACKGROUND AND SIGNIFICANCE

Background/Research Idea (DECAMP-1)

Repeat imaging for lung cancer screening frequently shows small indeterminate lung nodules, of which only a small fraction are malignant. Given the costs and complications associated with diagnostic workup of pulmonary nodules, effective tools are critically needed to distinguish patients with benign and malignant nodules. Such tools would allow for patients definitely diagnosed with lung cancer to more rapidly undergo treatment, and those without cancer to be spared the burden of invasive procedures. DECAMP seeks to determine the utility of minimally-invasive (airway biomarkers) and blood molecular biomarkers as follow up in patients with high-suspicion of lung cancer (comprising roughly 50% of patients suspected of lung cancer with other clinical findings). The challenge is to distinguish which patients with indeterminate pulmonary nodules actually have malignancy when the malignancy rate among all indeterminate nodules is as low as 10% to 20% (1).

The specific biomarkers that will be tested in this project are:

1) a multi-gene mRNA biomarker measured in cytologically normal large airway epithelial cells collected by bronchoscopy from the mainstem bronchus, a potential biomarker identified using genome-wide gene-expression profiling (2);
2) a multi-protein biomarker measured in bronchial biopsies collected by bronchoscopy, identified using MALDI-TOF MS (3);
3) a multi-protein biomarker measured in serum, identified using MALDI-TOF MS.51 (4); and
4) a multi-cytokine biomarker measured in serum, identified by profiling cytokines in important lung-cancer-related processes (5–8).

The fundamental conceptual innovation that links these biomarkers is the hypothesis that lung-cancer-related processes affect tissues that are distal to the site of disease, thereby allowing for the detection of lung cancer through multiple collection approaches—by bronchoscopy or in blood, sputum or urine. As these tissues are more proximal to the oral cavity, they can be collected less invasively than by biopsy of the suspect tumor itself from deep within the body cavity. The potential of less invasive approaches may enable lung cancer diagnosis in the setting of low-disease prevalence, such as this one, due to the low level of risk associated with assessing these biomarkers.

STUDY OBJECTIVES/SPECIFIC AIMS

DECAMP-1 aims to improve the efficiency of the diagnostic evaluation of patients with indeterminate pulmonary nodules. Biomarkers for lung cancer diagnosis measured in minimally invasive and non-invasive biospecimens may be able to distinguish between malignant or benign indeterminate pulmonary nodules in high-risk smokers.

Primary Aim

To determine the diagnostic accuracy of genomic and proteomic biomarkers in the airway and blood to detect lung cancer in the study cohort.

Secondary Aim

To evaluate the added diagnostic value of the molecular biomarkers to routine clinical and radiographic features used in diagnostic workup of pulmonary nodules.

PARTICIPANT SELECTION/ELIGIBILITY CRITERIA

Inclusion Criteria

- 45 years of age or older;
- Radiologic diagnosis of indeterminate pulmonary nodule (0.7 to 3.0 cm); must be of appropriate size at enrollment, but nodule(s) may have been first identified within 12 months prior;
- CT scan completed within 3 months prior to enrollment;
- Smoking status: Current or former cigarette smoker with ≥ 20 pack years (pack years = number of packs per day x number of years smoked)
- Willing to undergo fiberoptic bronchoscopy;

- Able to tolerate all biospecimen collection as required by protocol;
- Able to comply with standard of care follow up visits including clinical exams, diagnostic work-ups, and imaging for approximately two years from enrollment;
- Able to fill out Patient Lung History questionnaire;
- Willing and able to provide a written informed consent.

Exclusion Criteria

- History or previous diagnosis of lung cancer;
- Diagnosis of pure ground glass opacities for the target lesion (identified per Section 5.1.2 above) on chest CT (i.e., mixed features on the target lesion and pure ground glass opacity on non-target lesions are acceptable);
- Contraindications to nasal brushing or fiberoptic bronchoscopy, including: ulcerative nasal disease, hemodynamic instability, severe obstructive airway disease, unstable cardiac or pulmonary disease, inability to protect airway, or altered level of consciousness;
- Allergies to any local anesthetic that may be used to obtain biosamples in the study.

Inclusion of Women and Minorities

Both men and women and members of all ethnic groups are eligible for this study. In conformance with the National Institutes of Health (NIH) Revitalization Act of 1993, with regard to inclusion of women and minorities in clinical research, the projected gender and minority accruals are shown below:

Gender and Minority Accrual Estimates

Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	10	40	50
Not Hispanic or Latino	90	360	450
Ethnic Category: Total of all subjects	**100**	**400**	**500**
Racial Category			
American Indian or Alaskan Native	2	5	7
Asian	1	10	11
Black or African American	16	64	80
Native Hawaiian or other Pacific Islander	1	5	6
White	80	316	396
Racial Category: Total of all subjects	**100**	**400**	**500**

STUDY PROCEDURES

Patients who have been previously diagnosed with indeterminate pulmonary nodule(s) and who consent to participate in the ACRIN 4703 DECAMP-1 study will receive standard of care (SOC) treatment, including follow-up clinical exams, diagnostic work-ups, and imaging at their local institution for approximately two years from enrollment, or up until diagnosis of lung cancer. Imaging may include chest x-ray (CXR), chest CT, PET-CT, or other scans, as per institutional SOC. Other SOC procedures may include fine needle aspiration, percutaneous biopsy, or other methods of determining whether the pulmonary nodule(s) are benign or malignant.

After registration and consent, participants will submit biospecimen collections per protocol for biomarker analyses. ACRIN will arrange for the collection, processing, storage, shipping, distribution, and tracking of all biospecimens between participating clinical sites and the appropriate biorepositories. The ACR Imaging Core Laboratory will store all SOC imaging. The DECAMP consortium will coordinate data analyses of biospecimens, imaging, and clinical data. The DECAMP ACRIN 4703/ACRIN 4704 Biospecimen Procedure Manual will include specific procedures for the local institutions.

Study Procedures Table

Study Procedure	Eligibility/ Registration Visit	Biospecimen Collection	SOC Follow Up Visits *(Data collected annually)*	2-Year Follow-Up Visit (*if necessary to collect study completion data*)	Surgery *(if prescribed)*
Informed Consent Form	X				
Obtain Medical History	X				
Medical Record Review	X				
Screening/Eligibility Review	X				
Submit CT and Related Imaging to ACRIN (initial diagnosis/follow-up images)	X				
ACRIN Web Registration	X				
Site Radiologist Identifies Target Lesion on Institutional SOC Diagnostic Imaging	X				
Patient Lung History Questionnaire*	X				
Pulmonary function test		X	X		
Bronchoscopy: Brushing and Cell Collection Biopsy Tissue Collection		X			
Blood sample collection		X			
Blood sample processing by local site (with optional component)		X			
Urine sample collection		X			
Optional urine sample processing by local site		X			
Nasal brushing		X			
Buccal scraping		X			
Collect sputum samples		X			
AE Assessment		X	X		
Physical Examination (SOC)	X		X		
Diagnostic Work Up (SOC)			X		
Follow up imaging (SOC)			X		
Completion of Study Evaluation and Diagnosis Form by treating physician**			X**	X**	X
Surgery (SOC), if prescribed:					X
Surgical tissue collection (frozen and paraffin or 5-slide minimum)					X

* The Patient Lung Questionnaire must be completed in full during registration visit, starting it either before or after any same-day-as-consent biospecimen collection.

** The treating physician must complete a final Study Evaluation and Diagnosis Form at two years after enrollment to the study, or at the time of lung cancer diagnosis of the target lesion. Form completion may require an additional site visit. Additional source documentation may need to be collected, anonymized, and submitted to ACRIN if requested by the Adjudication Committee.