

NCCN/AstraZeneca Initiative Request for Proposals (RFP) in Patients with Early Stage Non-Small Cell Lung Cancer (NSCLC)

I. Introduction

National Comprehensive Cancer Network® (NCCN) and AstraZeneca Pharmaceuticals (AstraZeneca) are collaborating to offer a new funding opportunity seeking proposals to improve patient care and outcomes in early-stage non-small cell lung cancer (NSCLC). Multiple factors contribute to the complexity of treating the disease, including screening, staging, surgical options, and adjuvant systemic therapy.

The intent of this RFP is to encourage NCCN Member Institutions to submit letters of intent (LOIs) describing concepts and ideas for developing, implementing and evaluating healthcare provider performance and/or healthcare quality improvement initiatives to improve patient care and outcomes in early-stage NSCLC. Investigations aimed at understanding the current state and improving quality of early-stage NSCLC care at all time points along the clinical care continuum will be considered. Special consideration will be given to projects that address populations such as the elderly or underserved, the role of healthcare informatics, and innovation. Through improving the quality of cancer care, this RFP aims to improve translation of best practices and current data in early-stage NSCLC to the larger cancer community.

NCCN is a not-for-profit alliance of 30 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and accessible cancer care so patients can live better lives. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. By defining and advancing high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers around the world.

AstraZeneca has a deep-rooted heritage in oncology and offers a quickly-growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With six new medicines launched between 2014 and 2020, and a broad pipeline of small molecules and biologics in development, they are committed to advancing oncology focused on lung, ovarian, breast and blood cancers.

By harnessing the power of four scientific platforms – Immuno-Oncology, Tumor Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates – and by championing the development of personalized combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

AstraZeneca is also a founding member of the global [Lung Ambition Alliance](#), which has the goal of doubling lung cancer five-year survival by 2025.

This Request for Proposals (RFP) is issued by NCCN and is available only to applicants from NCCN Member Institutions. A review committee, led by NCCN, will make decisions on which proposals will receive funding. Funding will be provided by NCCN through support from AstraZeneca.

II. Background

Recent guidelines for staging and treatments of NSCLC, including immunotherapy and targeted therapies, have contributed to significant improvements in survival in the past 5 years. However, NSCLC remains the leading cause of cancer death in the United States, and the second most common cancer diagnosed in both men and women. NCCN has provided expert guidelines and particularly detailed clinical pathways for the staging and management of early-stage NSCLC for more than two decades.

Early-Stage NSCLC:

In 2021, there will be an estimated 235,760 cases of new lung cancer, with an estimated 116,000 deaths.¹ About 17% of patients will be diagnosed in the localized setting, stage I and stage II, and another 27% will be diagnosed in the regionally advanced setting, stage III.² There are a variety of curative and definitive treatment strategies for early-stage NSCLC including surgery, radiation, and adjuvant systemic treatments.

Screening for lung cancer has become a standard recommendation over the past 10 years based on the results of the National Lung Screening Trial (NLST) showing a 20% reduction in lung cancer mortality.³ In addition, the NELSON randomized CT screening trial from Europe was even more supportive with a mortality decrease 12-24% in males and 26-64% in females.⁴ The NCCN recommends lung cancer low-dose CT screening in patients with a ≥ 20 pack-years smoking history and over the age of 50.⁵ However, uptake of screening CT scans has been variable and underutilized in the clinical care setting. There are no biomarkers available for screening and selection of appropriate diagnostics for patients. There are several barriers that may affect the lack of screening such as necessary pre-visit documentation required for billing and patient preferences among others. Key components of a lung cancer screening program include providers and navigators trained to provide the proper documentation and counseling, smoking cessation program or education, and available clinicians needed to act on positive finding, such as a pathologist, pulmonologist, thoracic surgeon, radiologist and oncologist.

Staging: It is important to obtain the proper staging for patients with lung cancer. Patients found to have stage I NSCLC, and treated accordingly, can have a 5-year survival of up 76-92%, and 60% for stage II disease.⁶

Table 1 - Select Staging Techniques for Lung Cancer

Non-invasive	Invasive
CT chest with Contrast	Endobronchial ultrasound (EBUS)
PET/CT skull base to mid-thigh	Endoscopic ultrasound (EUS)
MRI brain	Mediastinoscopy
	Video Assisted or Robotic Assisted Thoracoscopic Surgery (VATS)

Non-invasive staging may be suggestive of nodal involvement; however, confirmatory invasive staging is preferred to determine the best definitive treatment strategies. There are several guidelines for staging recommendations in suspected early-stage NSCLC, however, they vary and a more inclusive standardization would be helpful for optimal care. Invasive staging techniques carry risk that can be

heightened in patients with certain co-morbid conditions. There are many quality gaps that exist in lung cancer staging. In a 2018 study, for all surgical patients regardless of stage, 34% underwent invasive staging. Rates of invasive staging among patients with clinical stage IB or greater or features suggestive of a central tumor were 43% and 52% (95% confidence interval: 50% to 54%), respectively.⁷ Recent data showed the rates of guideline-appropriate care did improve over the time frame 2004-2013 going from 23% to 34% with mediastinal sampling at any point during therapy increased from 54% to 64%.⁸

Adjuvant Treatment: Chemotherapy in the adjuvant setting was first recommended in and around 2004 with the International Adjuvant Lung Trial (IALT) showing for the first time, a small, but statistically significant improvement in overall survival (OS) for patients who received Cisplatin-based chemotherapy after surgery for early-stage NSCLC.⁹ Several additional randomized adjuvant chemotherapy trials matured over the next few years including NCI-C JBR-10 (Canada) and ANITA (Spain), resulting in the publication of the Lung Adjuvant Cisplatin Evaluation (LACE) meta-analysis which pooled 5 adjuvant trials and reported an overall benefit of 6.9% in lung cancer survival by adding adjuvant chemotherapy after surgery for stages I-III. There was no benefit for stage IA.¹⁰ Adjuvant chemotherapy for early-stage NSCLC has been standard of care for many years in eligible patients.

Adjuvant molecular targeted therapy has not been a standard practice. Recently, data reported from the ADAURA trial in 2020, for EGFR mutated NSCLC showed a significant DFS benefit in the post-surgical, post-chemotherapy adjuvant setting in favor of patient receiving the third generation EGFR inhibitor (EGFRI) osimertinib with a hazard ratio (HR) of 0.20 across stages IB-III A compared to placebo.¹¹ Overall survival data has not reached maturity. Given the clinically significant efficacy in terms of DFS, osimertinib has received FDA approval in the adjuvant early-stage NSCLC setting.

Molecular Testing in the Adjuvant Setting: In the metastatic NSCLC setting, data shows that over the years, molecular testing rates for non-squamous NSCLC have increased. However, data consistently shows inadequate testing rates discordant with the guidelines.¹² Several barriers exist to molecular testing including insufficient tissue, cost, time or patients/providers not wanting to wait for results, indifference to the benefit by the treating oncology team, logistical barriers, and several others.

Barriers are different in the adjuvant, early-stage NSCLC setting. For instance, insufficient tissue is unlikely to be a barrier given the availability of surgical specimen for NGS testing. Also, rapid turnaround time is not a requisite since patients will need time for postoperative recovery and potential adjuvant chemotherapy prior to determining whether or not they have an EGFR mutation that would make them eligible for adjuvant EGFRI therapy.

Conversely, new barriers may exist such as lack of knowledge of the newly approved targeted agent, concern for resources to test every surgical NSCLC specimen, cost, and logistics. Also, obtaining the medication from a specialty pharmacy, waiting for insurance prior authorizations and appeals, and finding help for high copays to afford the medication are all common obstacles to overcome to get the oral medication into a patient's hands. Another important barrier, seen often in other types of cancer, is patient motivation to take a daily pill, with potential toxicities, when there is no evidence of active disease.

Other Considerations: A multidisciplinary team (MDT) approach or a weekly tumor board meeting to discuss these cases can be very beneficial in the workup and management of early-stage NSCLC. In the current healthcare system, many larger healthcare systems are affiliated with satellite clinics, and there can be discrepancies in the care patterns between the larger institution and the satellite clinics. There

may be logistical barriers for smaller or satellite clinics to access these MDT meetings or approaches to care, thus affecting patient care. It is hopeful that advances in telemedicine may alleviate these quality issues.

Clinical treatment pathways are now also playing an increasingly important role in how providers manage NSCLC. While they can guide proper treatment selection, often physicians may feel pressured to choose a regimen in a pathway that may not be right for a certain patient. Most commercial pathway platforms give the provider several options and allow for reasonable explanations for going “off pathway” to use a particular treatment. However, there remains room for investigation into clinical pathways and how their outcomes measure up with other institutions who do not follow clinical pathways, both medically and financially. Furthermore, pathways could be expanded, to include symptom and toxicity management. Recent advent of ERAS (Enhanced Recovery after Surgery) programs have not only developed easy to adapt standardized patient care templates, but also have decreased lengths of stay, complications and opiate use. These are being expanded to peri-operative setting, including appropriate section and timing of adjuvant chemotherapy.

Finally, is there a role for healthcare informatics and innovation to help in this new area of adjuvant molecular targeted therapy? There are ongoing challenges in the standardization and logistics of molecular testing in NSCLC in the metastatic setting, despite targeted therapies being approved for over a decade. Molecular testing in the adjuvant setting introduces additional challenges as it requires coordination across numerous healthcare specialties. Artificial intelligence or other behavioral interventions may be implemented to enhance compliance and improve patient care.

III. Scope

The overall aim of this RFP is to develop innovative healthcare provider performance and/or quality improvement initiatives to improve patient care and outcomes in early stage NSCLC. It is anticipated that results from projects funded can be quickly disseminated to other practices and settings to rapidly improve delivery of cancer care. The goal is to provide funding to projects that, ultimately, are aimed at helping healthcare professionals deliver the best treatment to each patient at the optimal time.

This RFP is open to investigators from NCCN Member Institutions. The principal investigator must be from a NCCN Member Institution. Collaboration between NCCN Member Institutions and other institutions is strongly encouraged in order to foster the interactive sharing of knowledge and expertise, and to utilize the combined strengths of investigators. Funding for co-investigators will be routed through the NCCN Member Institution.

Only projects specific to the care of early stage NSCLC patients will be considered for funding.

The areas of emphasis identified for this RFP include the following:

1. Health Equity
 - a. Diversity and disparities in care patterns including testing
 - b. Disparity in screening for NSCLC
 - c. Barriers including but not limited to lack of healthcare provider knowledge, limited resources to perform the scanning, and trust in healthcare system

2. Screening
 - a. Novel methods including radiomics and other biomarkers
 - b. Understanding system barriers including providers and patients
3. Staging
 - a. Improving rates of guideline based clinical and pathologic staging
4. Adjuvant therapy for NSCLC
 - a. Patient-level motivation, compliance, education
 - b. Patient-Reported Outcomes (PRO's) in adjuvant therapy for NSCLC
 - c. Patient-level barriers, cost, social determinants of health
5. Molecular Profiling Patterns
 - a. Harmonization of molecular profiling and treatment selections
 - b. Biomarker selection, standardization
 - c. Improving testing algorithms, barriers, strategies
 - d. Role for germline testing, ancestral variation
6. Innovation and Informatics, including expanded ERAS Pathways
 - a. Support, critical pathway defaults
 - b. Systems prompts for CT screening at clinical level
 - c. Artificial Intelligence projects
7. Behavioral Economics
 - a. Identify and test interventions informed by behavioral economics to impact on clinician or patient behaviors to improve quality and outcomes
 - b. Identify innate or resistance mechanisms for provider-ordering patterns
 - c. Physician/Healthcare system behaviors and referral patterns
 - d. Integration of multi-disciplinary care

Areas of particular interest include:

1. Elderly Population
2. Underserved population
3. Rural Health via telemedicine

All funded proposals must:

1. Promote evidence-based care
2. Be sustainable after the award funding is complete
3. Collect data and report outcomes
4. Have a goal to enhance clinical outcomes, patient satisfaction, or provider satisfaction
5. Be flexible enough to address patient variability
6. Promote administrative and system efficiency

In addition, proposals that are scalable, reproducible, and quickly implementable, with tangible outcomes, are preferred. Ideally, proposed projects will offer a roadmap with a short runway to launch and demonstrate the ability to stick to timelines for deliverables.

Specific exclusions from this RFP include:

1. Therapeutic clinical trials
2. Preclinical studies
3. Significant overlap with previously funded studies

IV. Letters of Intent/Proposals

This RFP model employs a 2-stage process: Stage 1 is the submission of the 3-page LOI. If an LOI is selected, the applicant will be invited to Stage 2 to submit a full proposal.

Successful applicants will be able to describe the specific clinical practice gaps that exist for their own providers, health care system, or patient community and describe what they will do to close these gaps or problems. Site-specific obstacles to success should be identified and coupled with strategies to overcome the obstacles.

Programs must describe how the intervention, when implemented, will directly affect patient care and provide evidence of scalability (e.g., integration with an electronic medical record system), sustainability (e.g., plan for dissemination/applicability beyond the proposed institution), and can be completed within the timeframe specified.

The NCCN Request for Proposals Development Team (RFPDT) has been formed to oversee this process and will utilize a formalized review procedure to accept LOIs and subsequently select the proposals of highest scientific merit. The NCCN RFPDT oversaw the development of this RFP and will perform the peer review of applications.

V. Requirements

Date RFP Issued:	February 23, 2021
Clinical Area:	Early Stage Non-Small Cell Lung Cancer (NSCLC)
Target Audience:	Members of the health care team and administrators involved in the care of NSCLC cancer patients at NCCN Member Institutions.
Applicant Eligibility Criteria:	NCCN Member Institutions
Expected Approximate Monetary Range of Applications:	Total funding available is \$1.1 million. <ul style="list-style-type: none">• It is expected that 3-5 projects will be funded.• Individual projects requesting up to \$250,000.00 (including direct and 25% indirect cost) will be considered.• Smaller, lower-cost projects are strongly encouraged.

Estimated Key Dates:	<p>LOI Deadline: May 3, 2021 Please note the deadline is 5:00 PM Eastern Time.</p> <p>Anticipated LOI Notification Date: June 21, 2021</p> <p>Full Proposal Deadline*: August 2, 2021 *Only accepted LOIs will be invited to submit full proposals. Please note the deadline is 5:00 PM Eastern Time.</p> <p>Anticipated Full Proposal Notification Date: September 20, 2021</p>
Study Timeframes:	<p>Projects must be activated within 6 months, but no more than 9 months, from notification of approval.</p> <p>Period of Performance: Two years</p>
How to Submit:	<p>Please email LOI submission to NCCNLungProject@nccn.org</p> <p>IMPORTANT: Be advised LOIs submitted to the wrong email address or after the due date will not be reviewed by the committee.</p>
Selection Criteria:	<p>Applications will be evaluated on the basis of:</p> <ul style="list-style-type: none"> • Knowledge of and experience with the area; • Capability of carrying out the work; • Collaboration if appropriate; • Scalability and sustainability; • Potential effect and expected outcomes of the project; • Dissemination strategies.
Questions:	<p>If you have questions regarding this RFP, please direct them in writing to Nicole Kamienski at kamienski@nccn.org with the subject line “2021 NSCLC Project”.</p>
Mechanism by which Applicants will be Notified:	<p>All applicants will be notified via email by the anticipated dates noted above.</p> <p>Applicants may be asked for additional clarification if needed by the RFPDT.</p>

VI. Letter of Intent Submission Guidance

The LOI is a brief concept document that describes the proposed project at a **high level**. The Proposal Review Committee will select LOIs that are best aligned with the purpose of the RFP. All applicants will be notified with either an acceptance or a declination. Successful applicants will be asked to submit a full proposal for funding consideration.

LOIs should be single-spaced using Arial 11-point font and 1-inch margins. There is a 3-page limit for the main section and a 1-page limit for organizational detail. If extensive, references may be included on 1 additional page. Final submissions should not exceed 5 pages in total (3 pages for the main section, 1 page for organizational detail, and 1 page for references).

All required sections should be combined in one document (MS Word or Adobe PDF). There is no need to submit the organization detail or references in a document separate from the main section of the LOI.

Please note the formatting and page limit for the LOI. The LOI is inclusive of additional information of any kind. A submission exceeding the page limit **WILL BE REJECTED and RETURNED UNREVIEWED.**

LOIs should include the following sections:

Main Section (not to exceed 3 pages):

1. Project Title
2. Organization(s) involved
3. Principal Investigator
4. Focus of Project:
 - Program, tool, technology or clinical pathway
 - Addresses gaps in clinical practice
5. Goal and Objectives
 - Briefly state the overall goal of the project. Also describe how this goal aligns with the focus of the RFP and the goals of the applicant organization(s).
 - List the *overall* objectives you plan to meet with your project both in terms of learning and expected outcomes. Objectives should describe the target population as well as the outcomes you expect to achieve as a result of conducting the project.
6. Assessment of Need for the Project
 - Please include a quantitative baseline data summary, initial metrics (e.g., quality measures), or a project starting point (please cite data on gap analyses or relevant patient-level data that informs the stated objectives) in *your* target area. Describe the source and method used to collect the data. Describe how the data was analyzed to determine that a gap existed. If a full analysis has not yet been conducted, please include a description of your plan to obtain this information.
7. Target Audience
 - Describe the primary audience(s) targeted for this project. Also indicate whom you believe will directly benefit from the project outcomes. Describe the overall population size as well as the size of your sample population.
8. Project Design and Methods
 - Describe the planned project and the way it addresses the established need.
 - If your methods include educational activities, please describe succinctly the topic(s) and format of those activities.
9. Innovation
 - Explain what measures you have taken to assure that this project idea is original and does not duplicate other projects or materials already developed.

- Describe how this project builds upon existing work, pilot projects, or ongoing projects developed either by your institution or other institutions related to this project.

10. Evaluation and Outcomes

- In terms of the metrics used for the needs assessment, describe how you will determine if the practice gap was addressed for the target group. Describe how you expect to collect and analyze the data.
- Quantify the amount of change expected from this project in terms of your target audience.
- Describe how the project outcomes will be broadly disseminated.

11. Anticipated Project Timeline

12. Requested Budget

- A total amount requested is the only information needed for the LOI stage. **Full Budget is not required.** This amount can be adjusted at the Full Proposal stage as applicable.
- The budget amount requested must be in U.S. dollars (USD).
- While estimating your budget please keep the following items in mind:
 - i. Institutional overhead and indirect costs may be included within the request.
 - ii. The inclusion of these costs cannot cause the amount requested to exceed the budget limit set forth in the RFP.
 - iii. NCCN and its Member Institutions have an agreement to include a maximum of 25% indirect costs for projects funded by NCCN.

13. Additional Information

If there is any additional information you feel the SRC review committee should be aware of concerning the importance of this project, please summarize it in within the page limitations.

Organizational Detail (not to exceed 1 page):

Describe the attributes of the institutions/organizations/associations that will support and facilitate the execution of the project and the leadership of the proposed project. Articulate the specific role of each partner in the proposed project. Letters of support from partner organizations will be required at the Full Proposal stage only and should not be included with the LOI.

If a partnership is only proposed, please indicate the nature of the relationship in this section.

VII. Full Proposals

A limited number of applicants will be invited to submit for consideration a full proposal of no more than 10 pages, accompanied by a detailed, line-item budget. The full proposal format will be shared with the invitation to submit.

VIII. Terms and Conditions

This RFP does not provide permission and license for the use (including the creation of derivative products) of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for commercial use.

Funding recipients will need to maintain a separate end-user or other license agreement directly with NCCN for use of the NCCN Guidelines.

IV. References

1. CA Cancer J Clin 2021; 71: 7-33.
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3. NLST reference
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5. NCCN guidelines
6. Goldstraw P, et al. Journal of Thoracic Oncology, Volume 11, Issue 1, 2016, 39–51
7. Krantz SB, Howington JA, Wood DE, Kim KW, Kosinski AS, Cox ML et al. Invasive mediastinal staging for lung cancer by The Society of Thoracic Surgeons Database Participants. Ann Thorac Surg 2018; 106: 1055-62
8. Ost DE, Niu J, Zhao H, Grosu HB, Girodano SH. Quality gaps and comparative effectiveness in lung cancer staging and diagnosis. Chest 2020; 157 (5): 1322-1345
9. IALT study 2004
10. Pignon et al. J Clin Oncol 26:3552, 2008
11. ADUARA 2020
12. Gutierrez ME, Choi K, Lanman RB, et al. Genomic profiling of advanced non-small cell lung cancer in community settings: Gaps and opportunities. Clin Lung Cancer. 2017;18(6):651-659
13. RADIANT Trial, Kelly et al JCO 2015