



Educational Grant Request

Getting Tissue for Molecular Testing: A NSCLC Strategic Initiative

Temple University School of Medicine

Association of Community Cancer Centers (ACCC)

Fox Chase Cancer Center

MCM Education

TABLE OF CONTENTS

OVERALL AIM AND OBJECTIVES.....	2
TECHNICAL APPROACH	3
Current Assessment of Need in Target Area	4
Primary Audience.....	9
Intervention Design and Methods.....	9
Evaluation Design.....	12
DETAILED WORK PLAN AND DELIVERABLES SCHEDULE	13
References	15

1. OVERALL AIM AND OBJECTIVES

The Temple University School of Medicine (Temple) in collaboration with the Association of Community Cancer Centers (ACCC), Fox Chase Cancer Center and MCM Education propose a continuing medical education initiative on the topic of non-small cell lung cancer entitled ***Getting Tissue for Molecular Testing: A NSCLC Strategic Initiative***. The overall aim of this initiative is to improve how lung biopsies are performed in patients with NSCLC so that adequate tissue is available for molecular testing.

To accomplish this, Temple/Fox Chase/ACCC will recruit five (5) ACCC member organizations to participate in this initiative with Fox Chase Cancer Center being of the selected sites. Within each organization, we will identify baseline performance around: 1) percentage of NSCLC adenocarcinoma tumors that undergo molecular testing; 2) adequacy of lung biopsy samples for molecular testing; 3) types of protocols and workflow processes in place that are designed to increase molecular testing in patients with NSCLC; and 4) types of protocols and algorithms that are used by oncologists to guide the treatment of NSCLC patients based on molecular test data. The baseline data will be determined through the implementation of focus groups and surveys within each of the 5 centers and the use of available cancer registries.

The baseline data recently collected at Fox Chase, an NCI top rated cancer center, demonstrates the need to provide guidance and education to other centers about molecular testing. There were 1,700 new lung patients seen in the last calendar year and approximately 85% of lung cancer patients or 1,445 new patients had non-small cell histology. Our pathology department reports that 140 NSCLC patients had molecular testing in the last calendar year, representing only 10% of new NSCLC patients.

After obtaining and reviewing baseline data within each of the 5 organizations, a focused strategy will be tailored to each individual organization with the intent of increasing the percentage of lung biopsies that are adequate for molecular testing. The tactics to improve the percentage include a CME workshops lectures/presentations and tumor boards, the creation of task forces, process changes that leverage electronic health record capabilities, routine reminders/alerts, and other educational and process change activities. To assess the effectiveness of the tailored strategy within each organization and measure performance changes, outcomes data will be collected to at 6, 9, and 12 months.

The Learning Objectives for this initiative include:

1. Discuss the importance of obtaining adequate tissue samples at biopsy of patients with NSCLC in order to do molecular testing
2. Discuss the impact of an inadequate tissue sample on patient treatment and outcomes
3. Explain the challenges that may arise in obtaining an adequate tissue sample and strategies to overcome these challenges

4. Identify targeted treatments that would be indicated for patients with advanced NSCLC with positive biomarker findings
5. Explain how the identification of a *KRAS* gene mutation in a patient with advanced NSCLC would affect treatment strategy
6. Select optimal therapeutic options based on current evidence for the treatment of NSCLC with EGFR mutations and ALK gene rearrangements
7. Summarize recent data on investigational agents in development with the goal of overcoming mechanisms of resistance to inhibition of molecular signaling pathways.

2. TECHNICAL APPROACH

The primary role of TEMPLE will be in its responsibilities as an approved provider of continuing education for physicians. TEMPLE will serve an independent role in program planning. This role includes, but is not limited to, approval of program topics and NSCLC faculty; educational goals and learning objectives; and instructional and support materials.

Fox Chase Cancer Center is in the process of establishing reflex testing of all non-squamous NSCLC histologies for EGFR and KRAS status. ALK translocation testing will be done if KRAS and EGFR are negative. FCCC is also working towards expanding their panel of markers since more of our clinical trials require specific marker expression. Knowing the molecular status of patients who are referred to our centers will facilitate enrollment in trials and ensure that patients are receiving personalized care for their lung cancer treatment. Fox Chase with Director of Thoracic Medical Oncology Hossein Borghaei, MS, DO will be the lead center to participate in this initiative and will help shape future direction for other participating sites.

MCM Education, an established full-service medical education company, will provide comprehensive CME/CE educational support including content development, coordination of faculty and assisting in center recruitment with ACCC/Temple, timeline development and implementation and coordination of all educational components and project tasks related to each participating center and data collection and reporting. In the last year, MCM Education has been involved in developing 7 certified CME activities on NSCLC. 6 of the 7 activities focused on molecular biomarkers and we plan to incorporate outcomes data from these activities into this initiative.

The ACCC is currently in a multiyear study and report on molecular testing in the community setting. This project is not a clinical evaluation or education program, but rather looks at potential system barriers unique to the community setting that may slow or prevent the adaptation of testing. ACCC will provide overall guidance and approval of the faculty and clinical education interventions for this initiative and in the selection and recruitment process of the ACCC centers.

Example of ACCC potential participating sites:

Mount Carmel Health System, Mount Carmel Network Cancer Program, Columbus, Ohio	Lancaster General Health System, Lancaster, Pennsylvania
Virginia Cancer Institute, Richmond, Virginia	Harbin Clinic, Rome, Georgia
Seattle Cancer Care Alliance, Seattle, WA	Iowa Cancer Specialists, Davenport, Iowa

Example of FCCC Potential participating sites:

AtlantiCare Regional Medical Center, Egg Harbor Township, NJ	Crozer Keystone Health System, Upland, PA
Virtua Health, Voorhees, NJ	Pottstown Memorial Regional Cancer Center, Pottstown, PA

a. Current Assessment of Need in Target Area

Overview of Need

Lung cancer is the leading cause of cancer death in the United States. It is estimated that, in 2012, more than 226,000 people will be diagnosed with cancer, and of those patients, more than 160,000 will die from the disease.¹ Non-small cell lung cancer (NSCLC) is the most common lung cancer type, comprising approximately 85% of all lung cancer cases.² Certain genetic alterations have allowed the further classification of NSCLC into subsets. Mutations in the epidermal growth factor receptor (*EGFR*) gene been identified in up to 20% of NSCLC cases across the population and in up to 60% of NSCLC cases in the Asian population.^{3,4} Alterations in the anaplastic lymphoma kinase (*ALK*) gene have been estimated in up to 5% of NSCLC cases.⁵ Therapies are now available to target the signaling pathways associated with these genes, with important clinical ramifications. Clinicians who treat patients with NSCLC must have a current understanding of how *EGFR* and *ALK* genetic alterations affect treatment strategies and outcomes and of the importance of obtaining adequate tissue samples for biomarker testing.

Data Sources

The following sources were used to develop this assessment of need:

- 1) Medical literature review
- 2) Clinical trials data
- 3) Clinical practice guidelines^{6,7,8,9}
- 4) Outcomes data from previous CME/CE activities:
 - *A Multidisciplinary Approach to Advanced NSCLC: A Virtual Tumor Board Case Discussion* (October 2011-October 2012; N=482 clinicians as of 9/24/12, including physicians, physician assistants, and other clinicians with specialties including oncology, pathology, radiology, pulmonology, and surgery).¹⁰
 - *Biomarkers & Beyond: Redefining Systemic Therapy for NSCLC* (October 2011-January 2012; N=135 clinicians, including physicians, nurses, physician assistants, nurse practitioners, and other clinicians with specialties including oncology, pathology, and radiology).¹¹

- 5) Focused educational needs assessment survey on NSCLC (September 2012, N=52 clinicians, including medical, surgical, and radiation oncologists, interventional radiologists, pulmonologists, pathologists, oncology pharmacists, and other clinicians involved in the care of patients with NSCLC).¹²

Clinical Practice Gap 1

Pulmonologists, interventional radiologists, and pathologists are not consistently acquiring an adequate amount of tissue for *EGFR* molecular testing at the time of the initial biopsy of lesions that may be NSCLC. To improve outcomes for patients with NSCLC, oncologists are encouraged to focus increasingly more attention on the underlying molecular abnormalities in NSCLC.¹³ Molecular markers provide insight to help identify patients most likely to benefit from specific targeted therapies. Biomarkers have both prognostic and predictive values.^{6,14} Targeted therapies for the treatment of NSCLC include agents to block epidermal growth factor receptor (*EGFR*), anti-vascular endothelial growth factor (*VEGF*) angiogenesis inhibitors, and anaplastic lymphoma kinase (*ALK*) inhibitors.¹⁵ Tests for *EGFR* mutation and *EGFR* tyrosine kinase inhibitor sensitivity, as well as for abnormal *ALK* gene, are readily available.^{16,17} Use of the v-Ki-ras2 Kirsten rat sarcoma (*KRAS*) gene mutation test is also increasing and may be used as a predictive marker to identify NSCLC patients who are likely to have poor response from adjuvant chemotherapy or anti-*EGFR* therapies.^{18,19} Efficient testing for molecular subtypes is vital in determining appropriate and targeted NSCLC treatment, and limited tumor samples are a major challenge for molecular pathologists.^{20,21}

Barriers

- All oncology clinicians, including pulmonologists, interventional radiologists, and pathologists, need further knowledge about the utility of biomarker analysis in developing targeted NSCLC treatment approaches. Our needs assessment survey provides evidence for this clinical practice gap. In the survey, pulmonologists, interventional radiologists, and pathologists indicated lack of confidence in their knowledge of this topic, with only 17.4% rating their ability to “Describe NSCLC gene mutations and the utility of biomarker analysis in targeted treatment approaches to improve patient outcomes” as “very high,” and 39% self-rating this competency as medium, low, or very low. Among all clinicians who responded, only 15.4% rated their ability as “very high.” Also, in the survey, only 30.5% of pulmonologists, interventional radiologists, and pathologists rated their ability to “Discuss the value of testing initial biopsy specimens for EGFR mutations” as “very high,” and 39% self-rating this competency as medium, low, or very low. Among all clinicians who responded, only 28.8% rated their ability as “very high.”¹²
- All oncology clinicians, including pulmonologists, interventional radiologists, and pathologists, need to improve their understanding of the value of obtaining an adequate tissue sample in initial biopsy specimens for EGFR mutations testing. Our needs assessment survey provides evidence for this clinical practice gap. In the survey, only 34.8% of pulmonologists, interventional radiologists, and pathologists rated their ability to “Explain the importance of acquiring an adequate amount of tissue for *EGFR* molecular testing at the time of the initial biopsy of lesions that may be NSCLC” as “very high,” and 34.7% rated

this ability as medium, low, or very low.¹² Among all clinicians who responded, only 26.9% rated their ability as “very high,” with 40.4% reporting their ability as medium, low, or very low.¹² The size of a tissue sample to be used for mutations testing exceeds that of samples for cytologic or histologic needs, and getting a sample of adequate size can be challenging.²² In recent survey and focus group data collected by the Association of Community Cancer Centers (ACCC), providers indicated a lack of knowledge about adequate sample size for proper testing.

Clinical Practice Gap 2

Oncology clinicians involved in the care of patients with NSCLC are not consistently distinguishing between NSCLC patient subpopulations and providing individualized treatment based on the most current evidence-based clinical data. To improve outcomes for patients with NSCLC, oncologists are encouraged to focus increasingly more attention on the underlying molecular abnormalities in NSCLC.¹³ Recent updates to the National Comprehensive Cancer Network NSCLC clinical practice guidelines state the importance of pathologic evaluation in determining specific molecular abnormalities to predict sensitivity or resistance to an increasing number of targeted agents. The NCCN guidelines recommend that all patients with adenocarcinoma be tested for the *EGFR* mutation and for the *ALK* gene rearrangement.⁶ A recent ASCO provisional clinical opinion also emphasizes that patients with NSCLC should have their tumor tested for *EGFR* mutations to determine whether an *EGFR* tyrosine kinase inhibitor (TKI) or chemotherapy would be the appropriate first-line therapy.⁸ Even with these recommendations in place, it has been estimated that in the Temple University/Fox Chase Cancer Center oncology clinics, only ~10% of new patients with NSCLC received molecular testing in the last calendar year.²³ This low rate of molecular testing may not be unusual. Low use of molecular testing in NSCLC patients has been reported in a study presented at a 2011 conference sponsored by the American Association for Cancer Research.²⁴ In information gleaned through the ACCC survey and focus groups, most community based cancer programs expressed concerns around proper systems management for molecular testing. In addition, many community based providers did not know how many biopsies currently undergo molecular testing.

Barriers

- Oncology clinicians involved in the care of patients with NSCLC need additional knowledge, skills, and competency in distinguishing between NSCLC patient subpopulations. Our needs assessment survey provides multiple specific examples of evidence for this gap. In the survey, 55.8% of clinicians indicated a low level of confidence (self-rated competency of medium, low, or very low) in their ability to “Distinguish between NSCLC subpopulations in order to optimize therapeutic strategies.” Also, 48% of clinicians indicated a low level of confidence in their ability to “Describe the role of *EGFR* mutation testing in the management of NSCLC.”¹² Clinicians also indicated a low level of confidence in their ability to use specific patient criteria to determine optimal individualized NSCLC treatment approaches. In the survey, a high percentage of clinicians (percentages noted below) indicated a low level of confidence in their ability to list the criteria that would make

patients eligible for treatment with bevacizumab (57.6%), erlotinib (55.7%), crizotinib (57.7%), cetuximab (61.6%).¹²

- Oncology clinicians involved in the care of patients with NSCLC need additional knowledge, skills, and competency in providing optimal individualized treatment based on the most current evidence-based clinical data. Our needs assessment survey provides multiple specific examples of evidence for this gap. In the survey, a high percentage of clinicians (percentages noted below) indicated a low level of confidence in their ability to:¹²
 - Select therapeutic options for the treatment of NSCLC based on the most current evidence-based clinical data (50%).
 - Describe safety and tolerability issues with NSCLC treatments that often impact patient outcomes (48.1%).
 - Describe recent data on antiangiogenic therapies for NSCLC in combination with standard chemotherapy (67.3%).

Clinicians in the survey also indicated a low level of confidence in their ability to use specific targeted agents in individualized NSCLC treatment plans. In the survey, 37.5% of clinicians were unable to identify erlotinib as the agent most likely to benefit patients who have locally advanced or metastatic NSCLC with EGFR mutations, and 34.6% of clinicians were unable to identify crizotinib as the agent most likely to benefit patients who have locally advanced or metastatic NSCLC with ALK gene rearrangements.¹²

Outcomes data from previous CE/CME activities provide further evidence for this clinical practice gap:

- Outcomes data from the previous CE/CME activity *A Multidisciplinary Approach to Advanced NSCLC: A Virtual Tumor Board Case Discussion* provide further evidence for this gap. In the post-test for this program participants were asked “Which marker may be associated with sensitivity to cisplatin-based therapy for NSCLC?” Only 43% of participants were able to correctly identify ERCC1 and EGFR as the correct answer to this question.¹⁰
- Clinicians who participated in the CE/CME activity *Biomarkers & Beyond: Redefining Systemic Therapy for NSCLC* were asked to rate their level of agreement with this statement in the pre- and post-program surveys: “I feel comfortable making treatment decisions based on biomarker testing results.” While confidence related to this competency increased somewhat during the program, there is still significant room to improve clinician confidence in their ability to make treatment decisions based on biomarker testing results. After the program only 52% of respondents rated this competency in the top two choices on the “strongly agree” side of the scale.¹¹

Clinical Practice Gap 3

Many oncology clinicians involved in the care of patients with NSCLC are not prepared to incorporate new treatment approaches and emerging investigational therapies into individualized treatment plans for patients with NSCLC. As new evidence on cancer treatments emerges and new treatments become available, clinicians need guidance on whether or not to

change their practices in response to new research. The need for keeping clinicians up-to-date on therapeutic options will continue to increase. An impressive number of studies currently are seeking data for improving targeted NSCLC therapy. A search on “NSCLC” and “targeted” on ClinicalTrials.gov returns 198 studies, including a wide variety of approaches using targeted therapies in NSCLC.²⁵ Among new avenues being studied are: cell cycle kinase inhibitors;^{26,27} signal-transduction inhibitors, including ErbB receptor blockers;^{28,29} angiogenesis pathways beyond *VEGF*, including fibroblast growth factor receptors (*FGFR*) and platelet-derived growth factor receptors (*PDGFR*);^{30,31} and agents that inhibit Met proto-oncogene (*MET*) signaling.³²

Barriers

- The rapid pace of new discoveries in molecular mechanisms in NSCLC and targeted treatments presents a challenge in achieving timely dissemination of this information. Emerging clinical data continue to provide new evidence about optimal approaches for targeting the treatment of NSCLC. However, inadequate dissemination and implementation of relevant cancer-related research findings often lead to suboptimal care for cancer patients.³³ However, inadequate dissemination and implementation of relevant cancer-related research findings often lead to suboptimal care for cancer patients.³³ As new evidence on cancer treatments emerge and new treatments become available, clinicians need guidance on whether or not to change their practices in response to new research. Draft guidelines on the importance and use of biomarkers in lung cancer currently are being jointly developed by the College of American Pathologists (CAP), the International Association for the Study of Lung Cancer (IASLC), and the Association for Molecular Pathology (AMP). The guidelines state, “The discovery of the biologic and therapeutic importance of acquired genetic alterations in two genes that encode pharmacologically targetable tyrosine kinases involved in growth factor receptor signaling, *EGFR* and *ALK*, has changed the way these cancers are diagnosed and treated” and that the guidelines were developed to apprise oncology clinicians of recent changes “given the considerable published data on *EGFR*-mutant lung cancer and the rapid pace of work on *ALK*.”⁷ Emerging clinical data continue to provide new evidence about optimal approaches for targeting the treatment of NSCLC.

- Oncology clinicians involved in the care of patients with NSCLC need additional knowledge, skills, and competency in understanding the multiple mechanisms of NSCLC disease progression and emerging investigational agents with the potential to better target these mechanisms and thus improve patient outcomes. In the survey, a high percentage of clinicians (percentages noted below) indicated a low level of confidence in their ability to:¹²
 - Describe mechanisms of resistance to inhibition of molecular signaling pathways and the duration of response of approved pathway inhibitors (69.3%).
 - Discuss recent data on investigational agents in development with the goal of overcoming mechanisms of resistance to inhibition of molecular signaling pathways (63.5%).
 - Explain the signaling pathways in the development and progression of NSCLC and the consequences of dysregulation (69.7%).

- Explain the roles of proangiogenic signaling pathways in the development and progression of NSCLC (65.4%).
- Describe the impact of interactions between growth factors and their receptors on cellular proliferation, migration, differentiation, and cellular survival in NSCLC (63.5%).
- Describe ongoing research and recent data on clinical outcomes in advanced/metastatic NSCLC when inhibiting multiple proangiogenic signaling pathways (75%).

Conclusions

Because of a lack of knowledge among oncology clinicians regarding the need for biomarker testing and utilization of targeted treatment strategies in certain subsets of patients with advanced NSCLC, these patients are not always receiving the highest level of care. Obtaining an adequate amount of tissue to perform biomarker testing and identifying alterations in *EGFR* and *ALK* genes in these patients has important prognostic consequences, yet the number of patients who have the opportunity to take advantage of targeted treatment is alarmingly low. The goal of this continuing medical education activity is to impart this knowledge to oncology clinicians involved in the care of patients with NSCLC in order to give all patients their best chance at achieving positive and improved outcomes.

Primary Audience

The educational activities will be designed for oncologists, pathologists, thoracic surgeons, pulmonologists, interventional radiologists and other relevant healthcare professionals involved in the care of patients with NSCLC to close the professional practice gaps identified above. The interdisciplinary team at each center will participate in several workshops together and each discipline will also participate in activities tailored to their needs based on their role and clinical expertise in treating and managing lung cancer patients.

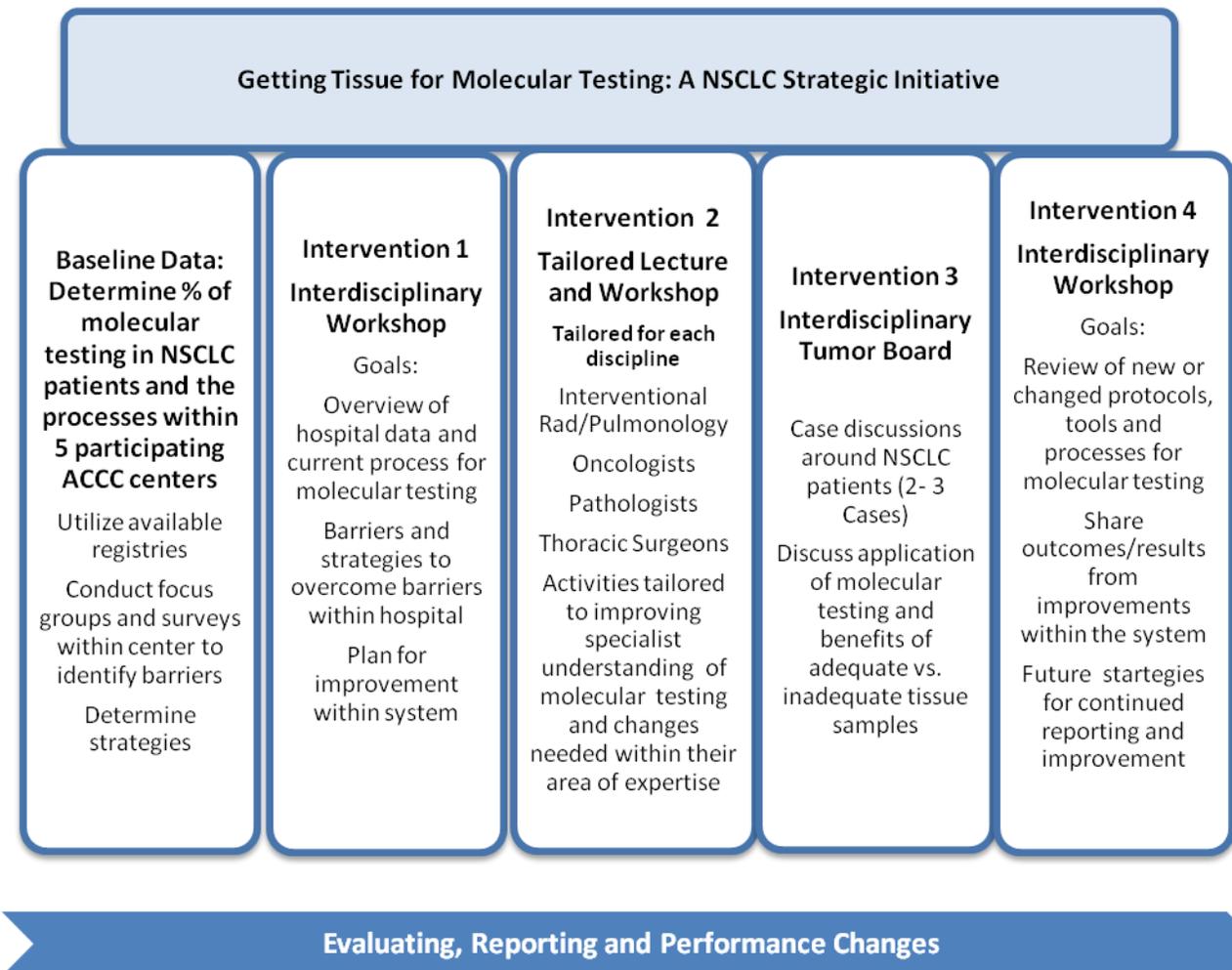
Pulmonologists and interventional radiologists, who perform lung biopsies, will receive educational activities and reminders that focus on the need to obtain enough tissue for molecular testing. We will identify viable process changes to remind clinicians to take a second biopsy if needed for molecular testing. Oncologist education will focus on the latest evidence supporting specific clinical treatment decisions based on molecular testing data. We will provide care plans and treatment algorithms for oncologists. We will identify viable process changes that will help pathologists ensure that NSCLC tissue samples are sent for molecular testing.

b. Intervention Design and Methods

Fox Chase Cancer Center and four additional centers will be recruited to participate in this initiative with assistance from ACCC. A lead physician or champion will be recruited at each of the centers to assist in the implementation of the improvement initiative and forming a taskforce. Once identified, we will conduct focus groups, survey the center and collect available cancer registry data to establish baseline data and report the current process, barriers and protocols in place for each center regarding molecular testing.

After obtaining baseline data within each of the 5 organizations, tailored strategies for each individual organization will be developed in order to increase the percentage of lung biopsies that are adequate for molecular testing. The tactics include working with each center champion to review the overall status of their center and establish the goals and objectives based on their reported baseline data. Additionally we will “train” the champion on the implementation of interventions to be delivered to their team of clinicians along with the desired outcomes and reporting process.

The CME activities will include workshops, lectures/presentations, and tumor boards along with the creation of task forces, process changes that leverage electronic health record capabilities, routine reminders/alerts, and other educational and process change activities. Outcomes data to measure performance changes will occur at 6, 9, and 12 months after the first intervention. MCM will develop content and slides for each of the proposed CME activities as well as the tools and other resources to be made available such as checklists, algorithms and protocols.



The proposed interventions developed and made available to each site include:

Intervention 1 –An interdisciplinary workshop lead by the faculty champion and /or other hospital faculty to provide an overview of data (where we are) and current process for molecular testing (what we are doing). Barriers will be identified and strategies to overcome these barriers within the cancer center will be presented along with a plan for improvement and measuring improvement (where we need to be and what we should be doing).

Intervention 2 – An activity tailored to improving specialist understanding of the impact of molecular testing on patients and changes needed within their area of expertise to improve outcomes.

- We will educate and remind those performing lung biopsies (pulmonologists and interventional radiologists) about the need to obtain enough tissue for molecular testing. We will identify viable process changes to remind clinicians to take a second biopsy if needed for molecular testing.
- We will educate oncologists about the latest evidence supporting specific clinical treatment decisions based on molecular testing data. We will provide care plans and treatment algorithms for oncologists.
- We will identify viable process changes that will help pathologists ensure that NSCLC tissue samples are sent for molecular testing.

Intervention 3 – An interdisciplinary Tumor Board activity discussing 2 - 3 NSCLC cases with the application of molecular testing and the benefits of adequate vs. inadequate tissue samples. Clinicians will be able to understand the impact of molecular testing on treatment selection and the overall patient outcomes as a result of their decisions and the system process.

Intervention 4 – An interdisciplinary follow-up activity to review new or changed protocols, tools and processes for molecular testing and share outcomes/results from improvements within the system. Future strategies for continued reporting and improvement will also be agreed upon.

System-specific process changes - These will be driven by task forces or committees within each organization. Examples of such changes will be presented and utilized as appropriate through the interventions. This may include: requisition forms for lung biopsies automatically include a check box for molecular testing; modifying order sets within computerized physician order entry systems; adding molecular marker fields to electronic health records; development of organization-specific care plans and treatment algorithms that are up-to-date, evidence-based, and that reflect the use of molecular test results for NSCLC patients.

c. Evaluation Design

MCM/Temple will develop evaluations, surveys and other tools to determine what improvements have been made at each of the 5 participating cancer centers. The cancer center registry, focus groups and surveys will quantify baseline performance within each organization as previously outlined. Each of the educational activities will include a pre/post/and follow-up survey to measure changes in physician behavior as they relate to: 1) ordering molecular tests when sending a lung biopsy; 2) checking for molecular test data before initiating treatment plans; 3) acting on the molecular test data to create or modify treatment plans; 4) communicating with other physicians to discuss the care of a patient. Additionally, a follow-up focus group and survey to measure process and system changes will be conducted at 10 - 12 months at each individual center.

Desired practice gap improvements that will be measured include:

- Pulmonologists, interventional radiologists, and pathologists *are consistently* acquiring an adequate amount of tissue for *EGFR* molecular testing at the time of the initial biopsy of lesions that may be NSCLC.
- Oncology clinicians involved in the care of patients with NSCLC *have improved in their ability and frequency* of distinguishing between NSCLC patient subpopulations and providing individualized treatment based on the most current evidence-based clinical data.
- Oncology clinicians involved in the care of patients with NSCLC *are incorporating new treatment approaches* and emerging investigational therapies into individualized treatment plans for patients with NSCLC.

Pre- and Post-Program Survey and Evaluation

Participants will be asked to complete a pre-program survey prior to the activity and a post-program survey, prior to completing the program evaluation. Based on identified program goals, the pre- and post-program surveys will measure attitudes, knowledge, behavior and confidence. The surveys will also allow for comparison of the effectiveness of the activity(s). The post-program evaluation will include questions regarding attainment of objectives, effectiveness of faculty, objectivity, scientific integrity, and predictive change in behavior as a result of the intervention.

Follow-Up Surveys

A personalized email message with a link to an electronic survey (post-program surveys) will be sent to all participants who provide valid contact information, approximately 30, 60, and 90 days-post activity. Post-program surveys will be designed to assess learning retention, as well as self-reported changes in clinician performance that may have occurred as a result of participation in the activity.

Outcomes Reporting

Interim reports including a detailed profile of the participating centers and aggregate participant metrics will be provided on a quarterly basis. In addition, a *Final Summative Report* will be generated at the conclusion of the series. The data collected at the end of the initiative will be compared to the baseline data at each participating center and shared during the final intervention so the task force can determine future direction and areas in need of continued improvement. The final report will include a detailed cancer center profile and analysis of all collected data with de-identified comments, as well as program faculty generated suggestions for future educational interventions on molecular testing. The program could then be sustained through internal funding within each organization.

Since the program will be disseminated throughout the FCCC and ACCC membership network, it would be scalable for other medical centers and hospitals that wish to follow similar processes. Key highlights and final outcomes from this initiative will be published and/or presented at major conferences that focus on areas such as: quality improvement, medical education, hospital education, oncology care, molecular testing, etc. (i.e. ASCO, ACCC, Alliance). Based on overall data, outcomes and system changes achieved, follow-up interventions may be proposed as a follow-up to this initiative.

Detailed Work Plan and Deliverables Schedule

Project Timeline

Actual milestones and target dates for completion are contingent upon receipt of a fully executed letter of agreement.

Activity	Responsibility				Timing				
	Temple	FC	ACCC	MCM	Q 1 13	Q 2	Q 3	Q 4	Q 1 14
Planning									
Telecon with all representatives of participating organizations and Dr. Bor to layout overall plan for development ,implementation and assigned tasks and deadlines	x	x	x	x	x				
Recruitment , approval and commissioning of faculty	x			x	x				
Faculty conference call	x	x	x	x	x				
Recruitment and approval of participating centers and identify champion	x		x	x	x	x			
Conduct focus groups, surveys and obtain baseline data from all 5 sites	x		x	x	x				
Report and analyze data to determine next steps	x	x	x	x	x				
Development									

Create Champion Guide/Training Manual	x	x		x	x				
Develop focus group questions and surveys	x	x		x	x				
Develop content/slides for initial workshop and lecture for each discipline (4)	x	x		x		x			
Develop Tumor Board cases/slides	x						x		
Develop final workshop activity and slides for each site	x			x				x	
Create a resource toolbox for centers	x	x		x		x	x		
Develop follow-up focus group questions	x							x	
Implementation									
Meet with each participating center to outline strategies and program implementation	x	x		x	x	x			
Workshop 1 delivered within each center	x	x		x		x			
Workshop 2 delivered for all disciplines all centers	x	x		x			x		
Tumor Board delivered all centers	x	x		x			x		
Workshop 3 delivered all centers	x	x		x				x	
Reporting and Outcomes									
Collect evaluations , pre/post program data on each activity	x			x		x	x	x	x
Collect and summarize reports from Champions	x			x		x	x	x	x
Interim report to Pfizer	x	x	x	x			x		
Conduct follow-up focus group and surveys at each center		x		x				x	
Final outcomes and reporting	x	x	x	x					x
Determine plan to publish/present data	x	x	x	x					x
Determine plan for phase 2 interventions needed at all sights	x								Q 2 14

References

- ¹ National Cancer Institute. SEER stat fact sheets: Lung and bronchus. Available at: <http://seer.cancer.gov/statfacts/html/lungb.html>. Accessed October 9, 2012.
- ² Sher T, Dy GK, Adjei AA. Small cell lung cancer. *Mayo Clin Proc.* 2008;83(3):355–367.
- ³ Pao W, Miller VA. Epidermal growth factor receptor mutations, small-molecule kinase inhibitors, and non-small-cell lung cancer: current knowledge and future directions. *J Clin Onc.* 2005;23:2556-2568.
- ⁴ Mok T, et al. Gefitinib or carboplatin–paclitaxel in pulmonary adenocarcinoma. *N Engl J Med.* 2009;361:947-957.
- ⁵ Sasaki T, et al. The biology and treatment of EML4-ALK non-small cell lung cancer. *Euro J of Cancer.* 2010;46:1773–1780.
- ⁶ National Comprehensive Cancer Network (NCCN) Web site. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) Non-Small Cell Lung Cancer Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed September 21, 2012.
- ⁷ College of American Pathologists (CAP)/International Association for the Study of Lung Cancer (IASLC)/Association for Molecular Pathology (AMP). Lung cancer biomarkers guideline draft recommendations. 2011. Available at: http://www.cap.org/apps/docs/membership/transformation/new/lung_public_comment_supporting_materials.pdf. Accessed October 4, 2012.
- ⁸ Keedy VL, Temin S, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: epidermal growth factor receptor (EGFR) Mutation testing for patients with advanced non-small-cell lung cancer considering first-line EGFR tyrosine kinase inhibitor therapy. *J Clin Oncol.* 2011;29(15):2121-2127.
- ⁹ Azzoli CG, Temin S, Aliff T, et al. 2011 Focused Update of 2009 American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non-Small-Cell Lung Cancer. *J Clin Oncol.* 2011 Sep 6. [Epub ahead of print]
- ¹⁰ Outcomes data from previous CE/CME activity: *A Multidisciplinary Approach to Advanced NSCLC: A Virtual Tumor Board Case Discussion*. Online presentation available from October 2011–October 2012; N=482 participants who completed post-program survey as of 9/24/12. Participants included physicians, physician assistants, and other clinicians with specialties including oncology, pathology, radiology, pulmonology, surgery, and others. Data on file at MCM Education.
- ¹¹ Outcomes data from previous CE/CME activity: *Biomarkers & Beyond: Redefining Systemic Therapy for NSCLC*. Series of grand rounds presentations from October 2011 to January 2012 and online activity available through December 2012; N=135 participants who completed post-program survey. Participants included physicians, nurses, physician assistants, nurse practitioners, and other clinicians with specialties including oncology, pathology, radiology, and others. Data on file at MCM Education.
- ¹² Focused educational needs assessment survey on NSCLC, September 2012, N=52 clinicians, including medical, surgical, and radiation oncologists, interventional radiologists, pulmonologists, pathologists, oncology pharmacists, and other clinicians involved in the care of patients with NSCLC. Data on file at MCM Education.
- ¹³ Argiris A, Gadgeel SM, Dacic S. Subdividing NSCLC: reflections on the past, present, and future of lung cancer therapy. *Oncology (Williston Park).* 2009;23(13):1147-1148, 1150.
- ¹⁴ Mino-Kunudson M, Mark EJ. Reflex testing for epidermal growth factor receptor mutation and anaplastic lymphoma kinase fluorescence in situ hybridization in non-small cell lung cancer. *Arch Pathol Lab Med.* 2011;135(5):655-664.
- ¹⁵ Saintigny P, Burger JA. Recent advances in non-small cell lung cancer biology and clinical management. *Discov Med.* 2012;13(7):287-297.
- ¹⁶ Idowu M, Fuller CE, Powers, CN. Non-small cell lung carcinoma: a diagnosis beyond its prime. *Pathol Case Rev.* 2009;14(5):199-205.
- ¹⁷ Drugs.com Web site. FDA approves Xalkori. August 26, 2011 news report. Available at: <http://www.drugs.com/newdrugs/fda-approves-xalkori-companion-diagnostic-type-late-stage-lung-cancer-2828.html>. Accessed September 21, 2012.
- ¹⁸ Riely GJ, Marks J, Pao W. KRAS mutations in non-small cell lung cancer. *Proc Am Thorac Soc.* 2009;6(2):201-205.
- ¹⁹ Wang S, An T, Wang J, et al. Potential clinical significance of a plasma-based KRAS mutation analysis in patients with advanced non-small cell

lung cancer. *Clin Cancer Res.* 2010;16(4):1324-1330.

²⁰ Ilie M, Hofman P. Pitfalls in lung cancer molecular pathology: how to limit them in routine practice? *Curr Med Chem.* 2012;19(16):2638-2651.

²¹ Aggarwal C, Somaiah N, Simon GR. Biomarkers with predictive and prognostic function in non-small cell lung cancer: ready for prime time? *J Natl Compr Canc Netw.* 2010;8(7):822-832.

²² Felip E, Gridelli C, Baas P, et al. Metastatic non-small-cell lung cancer: consensus on pathology and molecular tests, first-line, second-line, and third-line therapy: 1st ESMO Consensus Conference in Lung Cancer; Lugano 2010. *Ann Oncol.* 2011;22(7):1507-1519.

²³ Data on file at MCM Education. September 25, 2012.

²⁴ EGFR assay vastly underused in lung cancer patients. *The Oncology Report.* October 4, 2011. Available at: <http://www.oncologypractice.com/oncologyreport/news/patient-survivor-care/single-article/egfr-assay-vastly-underused-in-lung-cancer-patients/a56d2a08243fa45da5c706aedd524d2.html>. Accessed October 4, 2012.

²⁵ ClinicalTrials.gov Web site. Search of: "NSCLC" and "targeted." <http://www.clinicaltrials.gov/ct2/results?term=NSCLC+targeted&pg=1>. Accessed September 25, 2012.

²⁶ Sterlacci W, Fiegl M, Tzankov A. Prognostic and predictive value of cell cycle deregulation in non-small-cell lung cancer. *Pathobiology.* 2012;79(4):175-194.

²⁷ Medema RH, Lin CC, Yang JC. Polo-like kinase 1 inhibitors and their potential role in anticancer therapy, with a focus on NSCLC. *Clin Cancer Res.* 2011;17(20):6459-6466.

²⁸ Solca F, Dahl G, Zoephel A, et al. Target binding properties and cellular activity of afatinib (BIBW 2992), an irreversible ErbB family blocker. *J Pharmacol Exp Ther.* 2012 Aug 10. [Epub ahead of print]

²⁹ Miller VA, Hirsch V, Cadranell J, et al. Afatinib versus placebo for patients with advanced, metastatic, non-small-cell lung cancer after failure of erlotinib, gefitinib, or both, and one or two lines of chemotherapy (LUX-LUNG 1): a phase 2b/3 randomised trial. *Lancet Oncol.* 2012;13(5):523-538.

³⁰ Santos ES, Gomez JE, Ræz LE. Targeting angiogenesis from multiple pathways simultaneously: BIBF 1120, an investigational novel triple angiokinase inhibitor. *Invest New Drugs.* 2011 Feb 25 [Epub ahead of print]

³¹ Reck M, Kaiser R, Eschbach C, et al. A phase II double-blind study to investigate efficacy and safety of two doses of the triple angiokinase inhibitor BIBF 1120 in patients with relapsed advanced non-small-cell lung cancer. *Ann Oncol.* 2011; 22 (6): 1374-1381.

³² Belalcazar A, Azaña D, Perez CA, Ræz LE, Santos ES. Targeting the Met pathway in lung cancer. *Expert Rev Anticancer Ther.* 2012;12(4):519-528.

³³ Ousley AL, Swarz JA, Milliken EL, Ellis S. Cancer education and effective dissemination: information access is not enough. *J Cancer Educ.* 2010;25(2):196-205.