The Role of Histology and Molecular Markers in NSCLC

An innovative PI CME Initiative has implications for practice

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Historically, the only important decision-making point in lung cancer management used to be determining whether a tumor was small cell lung cancer (SCLC) or non-small lung cancer (NSCLC). However, it is now becoming increasingly evident that histologic and molecular characteristics are very important for making treatment decisions for patients with NSCLC. Clinical trials of targeted agents have yielded outcomes differences based on histologic subgroups, providing clinicians a rationale for histology-based treatment approaches. For example, several studies have indicated survival differences among patients with NSCLC in response to specific agents (e.g., pemetrexed, bevacizumab) based on histologic type of the tumor.[1-3]

Similarly molecularly targeted agents have demonstrated clinical activity in specific subsets of patients expressing the molecular targets. Epidermal growth factor receptor (EGFR) mutations are almost exclusively found in NSCLC adenocarcinomas, and the association of these mutations with clinical response to gefitinib and erlotinib has provided clinicians an opportunity to tailor treatment to the EGFR mutation profile of the tumor. A number of retrospective reviews and prospective trials have established that EGFR-inhibitor therapy leads to radiographic responses in approximately 75 to 80 percent of patients with EGFR mutation-positive NSCLC.[4]

An oncogenic fusion between echinoderm microtubule-associated protein-like 4 (EML4) and anaplastic lymphoma kinase (ALK) was recently identified in a small subset of NSCLC patients.[5] Like EGFR mutations, EML4-ALK gene fusions occur almost exclusively in adenocarcinoma and in female nonsmokers or light smokers.[6] Crizotinib, a recently approved drug targeting the EML4-ALK fusion protein, resulted in a dramatic regression or disappearance of tumor in 57 percent of patients harboring the EML4-ALK fusion gene and a 2-year survival of 54 percent.[7,8]

As histologic and molecular characteristics become increasingly important in treatment decision-making for patients with NSCLC, community oncologists need education on the role of histology and molecular biomarkers in personalizing therapy for patients with NSCLC.

PI CME Methodology

In this article, we describe a performance improvement (PI) continuing medical education (CME) initiative designed to improve adherence to evidence-based recommendation guidelines related to histologic and molecular testing for NSCLC. The strategic partners in this collaborative initiative (the Potomac Center for Medical Education, Rockpointe Division of Oncology, ACCC, and CE Outcomes, LLC) identified "improvement of physician performance with respect to the use of histologic and molecular data for guiding treatment decisions in patients with NSCLC" as the goal of the PI CME initiative. The initiative uses a two-part strategy:

Part one is a PI activity focused on a specific group of treating clinicians and their practices. Performance measures used to assess performance changes will be linked to all components of the PI CME activity through an online system. This will ensure robust data capture and ease of use for participants. Tools and resources will be provided to participants to implement the changes identified from the activity into clinical practice.

Part two will use strategies and methods devised by participants in the PI CME activity to design educational interventions, tools, and resources for the wider audience.

The results of this PI initiative will be described in a subsequent publication that will be published following data analysis.

Identifying QI Measures

There are few validated performance measures for NSCLC. Many established measures from such organizations as the Agency for Healthcare Research and Quality (AHRQ) and Quality Oncology Practice Initiative (QOPI) focus on time to treatment and surgical specifics, rather than treatment choice. ACCC assembled an expert panel to identify the quality improvement measures that can be assessed in this PI CME initiative. After careful consideration of the most recent clinical data available on this topic, national clinical practice guidelines

(NCCN and ASCO), and opinions of thought leaders in this field, the expert panel identified the following three quality improvement measures:

1. Percentage of patients diagnosed with NSCLC whose predominant histologic type was confirmed prior to initiation of treatment
2. Percentage of patients diagnosed with NSCLC who underwent EGFR and EML4-ALK testing prior to initiation of treatment
3. Percentage of patients diagnosed with NSCLC where adequate tissue was available from the initial biopsy for molecular testing.

This PI CME initiative will attempt to measure physician changes with respect to these three quality improvement measures. The aggregate data will be reviewed to assess the impact of the activity, uncover barriers, and to document successful strategies that participants employed to overcome the barriers. The information will be used to develop additional educational activities to educate a wider audience of oncologists.

Participant Eligibility & Recruitment

All practicing physicians involved in the treatment of patients with NSCLC are eligible to participate in this PI CME initiative. Potential participation benefits include:

- Obtaining 20 AMA PRA Category 1 credits for completing the PI CME Initiative
- Demonstrating experience in performance and quality improvement activities that will support Commission on Cancer (CoC) accreditation
- Having the ability to impact treatment standards in NSCLC within the practice and nationwide.

The goal is to recruit 100 participants to complete the PI CME initiative and 100 participants to serve as a baseline group to assess the barriers and perceptions of practicing oncologists involved in the treatment of patients with NSCLC. The data gathered from the baseline group will be used to refine the quality improvement measures, the assessment tools' content, the educational interventions, and as a comparison to the participant group for self-assessment.

The PI CME guides physicians through a three-stage process that enables them to easily collect and enter data from their own practices using self-assessments and chart reviews.

Stage A: Self-Assessment of Current Practice

Stage A consists of a self-assessment survey, patient chart data, personal goals, and an improvement plan. Using the self-assessment, participants will evaluate their knowledge, attitudes, and competence in the treatment of patients with NSCLC. In the chart abstraction section, participants enter information from 10 patient charts regarding patient age, gender, smoking status, and pathology tests ordered. The information will then be compared against the PI CME's proposed measures and guidelines. Participants will receive a personalized report of the self-assessment and chart abstraction portions of Stage A. The correct answer, along with supporting evidence and faculty commentary, will be displayed alongside each question and answer pair. The participant Action Plan will include:

- The educational interventions selected for each participant based on answers in the self-assessment and chart abstraction portion of Stage A
- A list of optional activities
- Tools and resources to aid in implementing the information contained in the interventions.

Participants may also add a personal goal, which will be included in the Action Plan. This plan will be displayed to participants each time they log into the system. Reports and certificates are automatically generated in the system and participants may reprint these documents at any time. At the completion of Stage A, participants will be awarded 5 AMA PRA Category 1 credits.™

Stage B: Educational Interventions

Participants will complete the educational activities recommended to them based on their performance in the Stage A self-assessment portion. The three educational interventions in this PI CME initiative are:

1. ***A webcourse.*** Two medical oncologists and a pathologist discuss a patient case regarding the diagnosis of the histologic and molecular subtype of NSCLC, factors for consideration in treatment, and treatment decision points supported by clinical evidence.
2. ***An online monograph.*** The monograph will consist of five short summaries of key clinical data presented and/or published related to the diagnosis, treatment, and management of patients with NSCLC, with an emphasis on histology and molecular testing.

Figure 1. Three-Stage PI CME Process

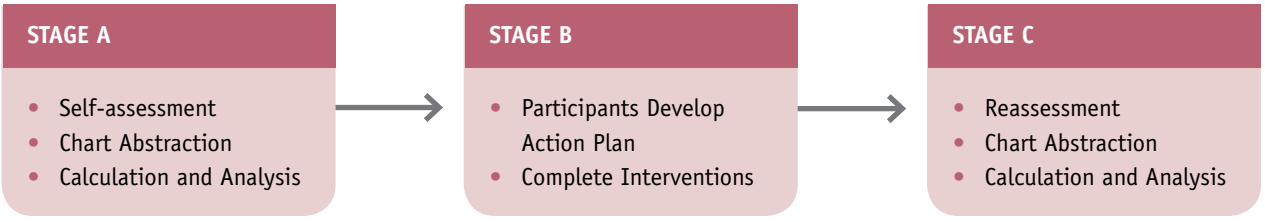
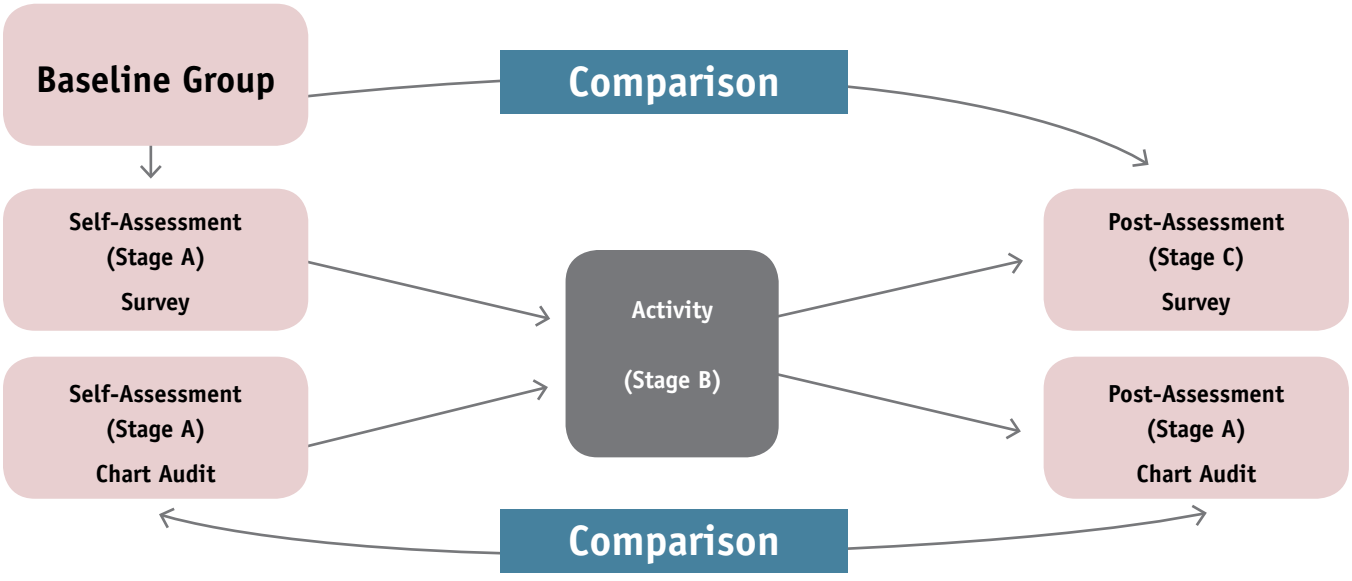


Figure 2. Study Design of the PI-CME Initiative



3. ***Online clinical challenge vignettes.*** Three vignettes will highlight unique aspects of the patient interaction that stimulated an interesting learning issue. All will focus on the application of histologic and molecular testing in the diagnosis and treatment of patients with NSCLC.

The PI CME activity will also include an expert commentary, providing participants with insight into the potential implications for practice change. Interactive questions will be interspersed throughout to track participant progress. Each educational intervention will include questions to assess practice patterns and changes in knowledge and competency of the participants. At the completion of Stage B, participants will be awarded 5 AMA PRA Category 1 credits™.

Stage C: Reassessment & Reflection on Practice

In Stage C, participants complete another self-assessment and enter data for 10 additional patient chart reviews (similar to Stage A), allowing participants to reflect and review their practice and compare against prior performance. Participants will receive a personalized report of the self-assessment and chart abstraction portions of Stage C. As in Stage A, the correct answer, along with supporting evidence and faculty commentary, will be displayed alongside each question and answer pair.

On completion of Stage C, participants will be awarded an additional 5 AMA PRA Category 1 credits™, for a total of 20 AMA PRA Category 1 credits.™

Data Analysis

Chi-squared ($\chi 2$) analyses will be performed on categorical data. T-tests will evaluate normally distributed continuous data. Comparisons of non-normally distributed continuous data are analyzed using the non-parametric Wilcoxon-Mann-Whitney test. The level of statistical significance is set at $p < 0.05$. All data will be presented in an aggregate form that does not reveal individual responses. Additionally, CE Outcomes, LLC, will calculate a Quality of Education Index (QoE)® score. This score is used to assess the summary impact of an educational activity on participant behavioral intentions, knowledge, and attitudes in a single reportable measure. OI

References

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