Consensus or Controversy?

Clinical Investigators Provide Perspectives on Targeted Treatment of Non-Small Cell Lung Cancer

CME Information

TARGET AUDIENCE

This activity is intended for hematologists, medical oncologists and other healthcare providers involved in the treatment of non-small cell lung cancer (NSCLC).

OVERVIEW OF ACTIVITY

Lung cancer is a devastating disease with broad-reaching impact on public health, as it accounts for 14% of all new cancer cases in the United States and the most cancer-related deaths among both men and women. Despite the many advances over the past few decades related to surgery, radiation therapy and chemotherapy, death rates attributable to lung cancer have remained relatively unchanged. Today, however, scientists and clinicians working in this area of cancer medicine have renewed optimism that these trends have started to change as recent research advances have led to an explosion in lung cancer genetic and biologic knowledge. A major focus of recent lung cancer research has been the development — and subsequent approval — of a number of molecular-targeted agents and the identification of related biomarkers to help guide treatment selection for those individuals who harbor specific oncogenic alterations.

These video proceedings from a CME symposium held during the 2016 IASLC Chicago MultidisciplInary Symposium in Thoracic Oncology feature discussions with leading researchers with an expertise in the management of lung cancer about clinical research findings relevant to treatment for patients with targetable tumor mutations to address existing uncertainties and help keep clinicians up to date and informed on the targeted treatment of NSCLC.

LEARNING OBJECTIVES

- Discriminate among molecular determinants that may be used to refine NSCLC prognosis and/or predict therapeutic response to an individual treatment, and apply available clinical guidelines to appropriately select patients for biomarker assessment.
- Recognize available and emerging research information validating the utility of blood-based diagnostic assays to identify or measure lung cancer biomarkers, and assess how, if at all, these testing platforms can be used by practicing oncologists outside of a research setting.
- Employ an understanding of personalized medicine to individualize the use of available EGFR inhibitors in the long-term care of patients with EGFR mutation-positive NSCLC.
- Describe mechanisms of tumor resistance to EGFR tyrosine kinase inhibitors (TKIs) and the clinical significance of T790M mutations, and discern how osimertinib can be optimally used for patients with progressive EGFR mutation-positive disease.
- Develop an understanding of the mechanisms of action, available research data and ongoing trials of investigational EGFR TKIs under development for the management of progressive EGFR-positive advanced NSCLC.
- Communicate the efficacy and safety of crizotinib, ceritinib, alectinib and other emerging ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK mutation testing.
- Assess new oncogenic pathways mediating the growth of unique NSCLC tumor subsets, and recall emerging data with experimental agents exploiting these targets.
- Recognize the advantages and limitations of multiplex and next-generation sequencing platforms, and determine their clinical and/or research application for patients with NSCLC.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 1.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity enables the participant to earn up to 1.25 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification

(MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at **ResearchToPractice.com/Privacy-Policy** for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/IASLC16/CME.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

MODERATOR

Joel W Neal, MD, PhD
Assistant Professor of Medicine
Division of Oncology
Stanford Cancer Institute
Stanford University
Palo Alto, California

Consulting Agreements: ARIAD Pharmaceuticals Inc, ARMO BioSciences, Boehringer Ingelheim Pharmaceuticals Inc, CARET/Physicians Resource Management, Clovis Oncology, Nektar; **Contracted Research:** ARIAD Pharmaceuticals Inc, ArQule Inc, Boehringer Ingelheim Pharmaceuticals Inc, Exelixis Inc, Genentech BioOncology, Merck, Nektar, Novartis Pharmaceuticals Corporation, Roche Laboratories Inc.

FACULTY

Geoffrey R Oxnard, MD
Lowe Center for Thoracic Oncology
Dana-Farber Cancer Institute
Assistant Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Advisory Committee: ARIAD Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Genentech BioOncology, Inivata, Takeda Oncology; **Consulting Agreements:** AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc.

Gregory J Riely, MD, PhD
Associate Attending
Memorial Sloan Kettering Cancer Center
New York, New York

Consulting Agreement: Genentech BioOncology; **Contracted Research:** ARIAD Pharmaceuticals Inc, Astellas Pharma Global Development Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc.

David R Spigel, MD
Program Director, Lung Cancer Research
Sarah Cannon Research Institute
Nashville, Tennessee

Advisory Committee: Bristol-Myers Squibb Company, Genentech BioOncology, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche Laboratories Inc; **Data and Safety Monitoring Board:** Merck.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

This activity is supported by educational grants from Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Foundation Medicine and Genentech BioOncology.

Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: September 2016

Expiration date: September 2017

Select Publications

Ahn MY et al. **Phase I study of AZD3759, a CNS penetrable EGFR inhibitor, for the treatment of non-small-cell lung cancer (NSCLC) with brain metastasis (BM) and leptomeningeal metastasis (LM).** *Proc ASCO* 2016;**Abstract 9003**.

Drilon AE et al. **Efficacy and safety of crizotinib in patients (pts) with advanced MET exon 14-altered non-small cell lung cancer (NSCLC).** *Proc ASCO* 2016;**Abstract 108**.

Drilon A et al. **Broad, hybrid capture-based next-generation sequencing identifies actionable genomic alterations in lung adenocarcinomas otherwise negative for such alterations by other genomic testing approaches.** *Clin Cancer Res* 2015;21(16):3631-9.

Drilon AE et al. **Phase II study of cabozantinib for patients with advanced RET-rearranged lung cancers.** *Proc ASCO* 2015;**Abstract 8007**.

Gainor JF et al. **EGFR mutations and ALK rearrangements are associated with low response rates to PD-1 pathway blockade in non-small cell lung cancer: A retrospective analysis.** *Clin Cancer Res* 2016;22(18):4585-93.

Jänne PA et al. **AZD9291 in EGFR inhibitor-resistant non-small-cell lung cancer.** *N Engl J Med* 2015;372(18):1689-99.

Kelly K et al. **Adjuvant erlotinib versus placebo in patients with stage IB-IIIA non-small-cell lung cancer (RADIANT): A randomized, double-blind, phase III trial.** *J Clin Oncol* 2015;33(34):4007-14.

Kris MG et al. **Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs.** *JAMA* 2014;311(19):1998-2006.

Lee CK et al. **Impact of specific epidermal growth factor receptor (EGFR) mutations and clinical characteristics on outcomes after treatment with EGFR tyrosine kinase inhibitors versus chemotherapy in EGFR-mutant lung cancer: A meta-analysis.** *J Clin Oncol* 2015;33(17):1958-65.

Neal JW et al. **Cabozantinib (C), erlotinib (E) or the combination (E+C) as second- or third-line therapy in patients with EGFR wild-type (wt) non-small cell lung cancer (NSCLC): A randomized phase 2 trial of the ECOG-ACRIN Cancer Research Group (E1512).** *Proc ASCO* 2015;**Abstract 8003**.

Nokihara H et al. **Alectinib (ALC) versus crizotinib (CRZ) in ALK-inhibitor naive ALK-positive non-small cell lung cancer (ALK+ NSCLC): Primary results from the J-ALEX study.** *Proc ASCO* 2016;**Abstract 9008**.

Oxnard GR et al. **Association between plasma genotyping and outcomes of treatment with osimertinib (AZD9291) in advanced non–small-cell lung cancer.** *J Clin Oncol* 2016;[Epub ahead of print].

Park K et al. **Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): A phase 2B, open-label, randomised controlled trial.** *Lancet Oncol* 2016;17(5):577-89.

Park K et al. **BI 1482694 (HM61713), an EGFR mutant-specific inhibitor, in T790M+ NSCLC: Efficacy and safety at the RP2D.** *Proc ASCO* 2016;**Abstract 9055**.

Planchard D et al. **Dabrafenib plus trametinib in patients with previously treated BRAF(V600E)-mutant metastatic non-small cell lung cancer: An open-label, multicentre phase 2 trial.** *Lancet Oncol* 2016;17(7):984-93.

Shaw AT et al. **Ceritinib in ALK-rearranged non-small-cell lung cancer.** *N Engl J Med* 2014;370(13):1189-97.

Wakelee HA et al. **E1505: Adjuvant chemotherapy +/- bevacizumab for early stage NSCLC — Outcomes based on chemotherapy subsets.** *Proc ASCO* 2016;**Abstract 8507**.

Wakelee HA et al. **Epidermal growth factor receptor (EGFR) genotyping of matched urine, plasma and tumor tissue from non-small cell lung cancer (NSCLC) patients (pts) treated with rociletinib.** *Proc ASCO* 2016;**Abstract 9001**.

Yang JC et al. **Osimertinib activity in patients with leptomeningeal (LM) disease from non-small cell lung cancer (NSCLC): Updated results from BLOOM, a phase I study.** *Proc ASCO* 2016;**Abstract 9002**.

Yang JC et al. **Afatinib versus cisplatin-based chemotherapy for EGFR mutation-positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): Analysis of overall survival data from two randomised, phase 3 trials.** *Lancet Oncol* 2015;16(2):141-51.

Yu HA et al. **Antitumor activity of ASP8273 300 mg in subjects with EGFR mutation-positive non-small cell lung cancer: Interim results from an ongoing phase 1 study.** *Proc ASCO* 2016;**Abstract 9050**.