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 15% of all new cancer cases in the US and the most cancer-related deaths among both men and women. In the year 2015, it is estimated that 221,200 individuals will be diagnosed and 158,040 individuals will die from the disease. 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, there is 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 among scientists and clinicians working in this area of cancer medicine. 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 in conjunction with the 16th World Conference on Lung Cancer feature discussions with leading researchers regarding actual cases of patients with NSCLC and tumor driver mutations from the practices of general medical oncologists and related clinical research findings 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.
- Employ an understanding of personalized medicine to individualize the use of available EGFR inhibitors in the long-term management of EGFR mutation-positive NSCLC.
- Describe mechanisms of tumor resistance to EGFR tyrosine kinase inhibitors (TKIs), and identify investigational therapeutic opportunities to circumvent this process.
- Communicate the efficacy and safety of crizotinib, ceritinib and other emerging ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK and ROS1 mutation testing.
- Consider available clinical data and investigator perspectives when caring for patients with EGFR- or ALK-positive NSCLC and brain metastases.
- Assess new oncogenic pathways mediating the growth of unique NSCLC tumor subsets, and recall emerging data with experimental agents exploiting these targets.
- Recognize the abilities and limitations of multiplex and next-generation sequencing platforms, and determine their clinical and/or research application for patients with NSCLC.
- Appreciate the scientific rationale for ongoing investigation of novel agents or therapeutic approaches in NSCLC, and counsel appropriately selected patients about study participation.

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CREDIT DESIGNATION STATEMENT
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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 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/IASLCMutations15/CME.
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CONSULTING ONCOLOGISTS — Drs Fishkin, Harwin and Simmons have no real or apparent conflicts of interest to disclose.

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**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

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**Expiration date:** November 2016
Mark G Kris, MD


ENSURE: A multicenter, open-label, randomized phase III study to evaluate the efficacy and safety of erlotinib (Tarceva®) versus gemcitabine/cisplatin as the first-line treatment for stage IIIb/IV non-small cell lung cancer (NSCLC) patients with mutations in the tyrosine kinase domain of epidermal growth factor receptor (EGFR) in their tumors. NCT01342965


Kelly K et al. A randomized, double-blind phase 3 trial of adjuvant erlotinib (E) versus placebo (P) following complete tumor resection with or without adjuvant chemotherapy in patients (pts) with stage IB-IIIA EGFR positive (IHC/FISH) non-small cell lung cancer (NSCLC): RADIANT results. Proc ASCO 2014;Abstract 7501.


LUX-Lung 6: A randomized, open-label, phase III study of BIBW 2992 versus chemotherapy as first-line treatment for patients with stage IIIB or IV adenocarcinoma of the lung harbouring an EGFR activating mutation. NCT01121393


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Park K et al. Updated safety and efficacy results from phase I/II study of HM61713 in patients (pts) with EGFR mutation positive non-small cell lung cancer (NSCLC) who failed previous EGFR-tyrosine kinase inhibitor (TKI). *Proc ASCO* 2015;Abstract 8084.


Yu HA et al. Phase I dose escalation study of ASP8273, a mutant-selective irreversible EGFR inhibitor, in subjects with EGFR mutation positive NSCLC. *Proc ASCO* 2015;Abstract 8083.


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A phase 1, two-part, multi-center, non randomized, open-label, multiple dose first-in-human study of DS-6051b, an oral ROS1 and NTRK inhibitor, in subjects with advanced solid tumors. NCT02279433

An open-label, multicenter, global phase 2 basket study of entrectinib for the treatment of patients with locally advanced or metastatic solid tumors that harbor NTRK1/2/3, ROS1, or ALK gene rearrangements. NCT02568267


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Gettinger SN et al. Brigatinib (AP26113) efficacy and safety in ALK+ NSCLC: Phase 1/2 trial results. Proc WCLC 2015;Abstract 33.06.


Phase 1/2 study of PF 06463922 (an ALK/ROS1 tyrosine kinase inhibitor) in patients with advanced non-small cell lung cancer harboring specific molecular alterations. NCT01970865

PROFILE 1001: Phase 1 safety, pharmacokinetic and pharmacodynamic study of PF-02341066, a c-MET/HGFR selective tyrosine kinase inhibitor, administered orally to patients with advanced cancer. NCT00585195

PROFILE 1014: Phase 3, randomized, open-label study of the efficacy and safety of crizotinib versus pemetrexed/cisplatin or pemetrexed/carboplatin in previously untreated patients with non-squamous carcinoma of the lung harboring a translocation or inversion event involving the anaplastic lymphoma kinase (ALK) gene locus. NCT01154140

Shaw A et al. Clinical activity and safety of PF-06463922 from a dose escalation study in patients with advanced ALK+ or ROS1+ NSCLC. Proc ASCO 2015;Abstract 8018.

Shaw A et al. Ceritinib (LDK378) for treatment of patients with ALK-rearranged (ALK+) non-small cell lung cancer (NSCLC) and brain metastases (BM) in the ASCEND-1 trial. Proc SNO 2014;Abstract BM-32.


Tony SK Mok, MD


Planchard D et al. Interim results of a phase II study of the BRAF inhibitor (BRAFi) dabrafenib (D) in combination with the MEK inhibitor trametinib (T) in patients (pts) with BRAF V600E mutated (mut) metastatic non-small cell lung cancer (NSCLC). Proc ASCO 2015;Abstract 8006.
