THE NEW BIOLOGY OF NON-SMALL CELL LUNG CANCER

TARGET AUDIENCE
This activity is intended for medical oncologists and other healthcare providers involved in the treatment of lung cancer.

OVERVIEW OF ACTIVITY
Lung cancer is a devastating disease with a broad-reaching impact on public health, accounting for 14% 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. Importantly, 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, many are optimistic that these trends have already 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.

To bridge the gap between research and patient care, this video presentation by Dr. Heather Wakelee uses a review of recent relevant publications and presentations, ongoing clinical trials and clinical investigator treatment preferences to assist medical oncologists and other healthcare providers involved in the treatment of lung cancer with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES
• Discriminate among molecular determinates that may be used to refine non-small cell lung cancer (NSCLC) prognosis and/or predict therapeutic response to an individual treatment.
• Employ an understanding of personalized medicine to individualize the use of available EGFR inhibitors in the treatment of NSCLC.
• Describe mechanisms of tumor resistance to EGFR tyrosine kinase inhibitors (TKIs), and identify investigational therapeutic opportunities to circumvent these processes.
• Communicate the efficacy and safety of crizotinib, ceritinib (LDK378) and other investigational ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK mutation testing.
• Describe emerging data on the efficacy and safety of tumor immunotherapy directed at the PD-1/PD-L1 pathway in lung cancer, and consider this information when counseling patients regarding clinical trial participation.
• Recognize the results of recently completed Phase III trials examining the efficacy and safety of the novel monoclonal antibodies necitumumab and ramucirumab for patients with advanced NSCLC.
• Assess new oncogenic pathways mediating the growth of unique NSCLC tumor subsets, and recall emerging data with experimental agents exploiting these targets.

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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/GrandRoundsLung15/CME.

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

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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

**Last review date:** October 2015

**Expiration date:** October 2016
A phase III double-blind trial for surgically resected early stage non-small cell lung cancer: Crizotinib versus placebo for patients with tumors harboring the anaplastic lymphoma kinase (ALK) fusion protein. NCT02201992

A randomized phase II study of individualized combined modality therapy for stage III non-small cell lung cancer (NSCLC). NCT01822496

A randomized phase II trial of erlotinib alone or in combination with bevacizumab in patients with non-small cell lung cancer and activating epidermal growth factor receptor mutations. NCT01532089

Adjuvant lung cancer enrichment marker identification and sequencing trial. NCT02194738


CheckMate 017: An open-label randomized phase III trial of BMS-936558 (nivolumab) versus docetaxel in previously treated advanced or metastatic squamous cell non-small cell lung cancer (NSCLC). NCT01642004

CheckMate 026: An open-label, randomized, phase 3 trial of nivolumab versus investigator’s choice chemotherapy as first-line therapy for stage IV or recurrent PD-L1+ non-small cell lung cancer. NCT02041533

CheckMate 057: An open-label randomized phase III trial of BMS-936558 (nivolumab) versus docetaxel in previously treated metastatic non-squamous non-small cell lung cancer (NSCLC). NCT01673867


Drilon A et al. Next-generation sequencing (NGS) to identify actionable genomic alterations (GA) in “pan-negative” lung adenocarcinomas (ADC) from patients with no smoking or a light smoking (NS/LS) history. Proc ASCO 2014;Abstract 8029.


Garon EB et al. Antitumor activity of pembrolizumab (Pembro; MK-3475) and correlation with programmed death ligand 1 (PD-L1) expression in a pooled analysis of patients (pts) with advanced non-small cell lung. Proc ESMO 2014;Abstract LBA43.

Garon EB et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): A multicentre, double-blind, randomised phase 3 trial. Lancet 2014;384(9944):665-73.


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.

KEYNOTE-010: A phase II/III randomized trial of two doses of MK-3475 (SCH900475) versus docetaxel in previously treated subjects with non-small cell lung cancer. NCT01905657
KEYNOTE-024: A randomized open-label phase III trial of MK-3475 versus platinum based chemotherapy in 1L subjects with PD-L1 strong metastatic non-small cell lung cancer. NCT02142738

KEYNOTE-042: A randomized, open label, phase III trial of overall survival comparing pembrolizumab (MK-3475) versus platinum based chemotherapy in treatment naive subjects with PD-L1 positive advanced or metastatic non-small cell lung cancer. NCT02220894


Lung-MAP: S1400 phase II/III biomarker-driven master protocol for second line therapy of squamous cell lung cancer. NCT02154490

LUX-Lung 3: A randomised, 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. NCT00949650

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 stage IIIB or IV adenocarcinoma of the lung harbouring an EGFR activating mutation. NCT01121393

Mok T et al. Gefitinib/chemotherapy vs chemotherapy in epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC) after progression on first-line gefitinib: The Phase III, randomised IMPRESS study. *Proc ESMO* 2014;Abstract LBA2_PR.


RADIANT: A multi-center, randomized, double-blind, placebo-controlled, phase 3 study of single-agent Tarceva® (erlotinib) following complete tumor resection with or without adjuvant chemotherapy in patients with stage IB-IIIA non-small cell lung carcinoma who have EGFR-positive tumors. NCT00373425

Randomized double blind placebo controlled study of erlotinib or placebo in patients with completely resected epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC). NCT02193282

REVEL: A randomized, double-blind, phase 3 study of docetaxel and ramucirumab versus docetaxel and placebo in the treatment of stage IV non-small cell lung cancer following disease progression after one prior platinum-based therapy. NCT01168973


Rizvi NA et al. Clinical trials of MPDL3280A (anti-PDL1) in patients (pts) with non-small cell lung cancer (NSCLC). *Proc ASCO* 2014;Abstract TPS8123.


