NEW AGENTS AND CLINICAL STRATEGIES IN THE SYSTEMIC TREATMENT OF NON-SMALL CELL LUNG CANCER

CME Information

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 13% of all new cancer cases in the US and the most cancer-related deaths among both men and women. In the year 2016, it is estimated that 224,390 individuals will be diagnosed and 158,080 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 Mark A Socinski 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, and identify investigational therapeutic opportunities to circumvent these processes.
- Communicate the efficacy and safety of crizotinib, ceritinib and other investigational ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK mutation testing.
- Describe available and 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 protocol and nonresearch options.
- Appreciate the recent FDA approval of nivolumab and pembrolizumab, and optimally employ these novel immunotherapeutic agents in the management of metastatic NSCLC.
- Recognize the recent FDA approval of ramucirumab for progressive metastatic NSCLC, and discern how this agent can be optimally integrated into clinical practice for patients with squamous and nonsquamous disease.
- 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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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 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

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Select Publications

Brahmer J et al. **Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer.** *N Engl J Med* 2015;373(2):123-35.

Camidge DR et al. **Efficacy and safety of crizotinib in patients with advanced c-MET-amplified non-small cell lung cancer (NSCLC).** *Proc ASCO* 2014;**Abstract 8001**.

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.

Garon EB et al; KEYNOTE-001 Investigators. **Pembrolizumab for the treatment of non-small-cell lung cancer.** *N Engl J Med* 2015;372(21):2018-28.

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.

Herbst RS et al. **Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): A randomised controlled trial.** *Lancet* 2016;387(10027):1540-50.

Janjigian YY et al. **Dual inhibition of EGFR with afatinib and cetuximab in kinase inhibitor-resistant EGFR-mutant lung cancer with and without T790M mutations.** *Cancer Discov* 2014;4(9):1036-45.

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

Keir ME et al. **PD-1 and its ligands in tolerance and immunity.** *Annu Rev Immunol* 2008;26:677-704.

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.

Ou SHI et al. **Efficacy and safety of the ALK inhibitor alectinib in ALK+ non-small-cell lung cancer (NSCLC) patients who have failed prior crizotinib: An open-label, single-arm, global phase 2 study (NP28673).** *Proc ASCO* 2015;**Abstract 8008**.

Pardoll DM. **The blockade of immune checkpoints in cancer immunotherapy.** *Nat Rev Cancer* 2012;12(4):252-64.

Paz-Ares L et al. **Phase III, randomized trial (CheckMate 057) of nivolumab (NIVO) versus docetaxel (DOC) in advanced non-squamous cell (non-SQ) non-small cell lung cancer (NSCLC).** *Proc ASCO* 2015;**Abstract LBA109**.

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**.

Sequist LV et al. **Rociletinib in EGFR-mutated non-small-cell lung cancer.** *N Engl J Med* 2015;372(18):1700-9.

Seto T et al. **Erlotinib alone or with bevacizumab as first-line therapy in patients with advanced non-squamous non-small-cell lung cancer harbouring EGFR mutations (JO25567): An open-label, randomised, multicentre, phase 2 study.** *Lancet Oncol* 2014;15(11):1236-44.

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

Soria JC et al. **Gefitinib plus chemotherapy versus placebo plus chemotherapy in EGFR-mutation-positive non-small-cell lung cancer after progression on first-line gefitinib (IMPRESS): A phase 3 randomised trial.** *Lancet Oncol* 2015;16(8):990-8.

Spigel DR et al. **A phase III study (CheckMate 017) of nivolumab (NIVO; anti-programmed death-1 [PD-1]) vs docetaxel (DOC) in previously treated advanced or metastatic squamous (SQ) cell non-small cell lung cancer (NSCLC).** *Proc ASCO* 2015;**Abstract 8009**.

Spira AI et al. **Efficacy, safety and predictive biomarker results from a randomized phase II study comparing MPDL3280A vs docetaxel in 2L/3L NSCLC (POPLAR).** *Proc ASCO* 2015;**Abstract 8010**.

Thatcher N et al; SQUIRE Investigators. **Necitumumab plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone as first-line therapy in patients with stage IV squamous non-small-cell lung cancer (SQUIRE): An open-label, randomised, controlled phase 3 trial.** *Lancet Oncol* 2015;16(7):763-74.

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.