CONSENSUS OR CONTROVERSY: Clinical Investigators Provide Perspectives on Targeted Treatment of Metastatic 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 13% 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. This has created a paradigm shift in the way patients with advanced NSCLC are initially stratified and counseled, moving from a "one-size-fits-all" approach to a customized, biomarker-driven treatment algorithm. Significantly, this has also created an imperative for clinicians to appropriately and actively attempt to identify and subsequently treat specific patients.

These video proceedings from a CME symposium held during the 2017 Multidisciplinary Thoracic Cancers Symposium 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/measure lung cancer biomarkers, and assess how, if at all, these testing platforms can be used by practicing oncologists outside of a research setting.
- Recognize the abilities and limitations of multiplex and next-generation sequencing platforms, and determine their clinical and/or research application for patients with NSCLC.
- Employ an understanding of personalized medicine to individualize the use of available EGFR tyrosine kinase inhibitors (TKIs) in the long-term management of EGFR mutation-positive NSCLC.
- Describe mechanisms of tumor resistance to EGFR TKIs and the clinical significance of T790M mutations, and discern how available and investigational therapies can be optimally employed in the protocol and nonresearch care of patients with progressive EGFR mutation-positive disease.
- Communicate the efficacy and safety of approved and other emerging ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK mutation testing.
- Assess newly recognized oncogenic pathways mediating the growth of unique NSCLC tumor subsets, and recall emerging data with experimental agents exploiting these targets.

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FACULTY — The following faculty (and their spouses/partners) reported relevant 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

A Phase 3 multicenter open-label study of brigatinib (AP26113) versus crizotinib in patients with ALK-positive advanced lung cancer. NCT02737501

A Phase III, double-blind, randomised study to assess the safety and efficacy of AZD9291 versus a standard of care epidermal growth factor receptor tyrosine kinase inhibitor as first line treatment in patients with epidermal growth factor receptor mutation positive, locally advanced or metastatic non small cell lung cancer. NCT02296125

A Phase III, double-blind, randomized, placebo-controlled multi-centre, study to assess the efficacy and safety of AZD9291 versus placebo, in patients with epidermal growth factor receptor mutation positive Stage IB-IIIA non-small cell lung carcinoma, following complete tumour resection with or without adjuvant chemotherapy (ADAURA). NCT02511106

Aisner D et al. **Effect of expanded genomic testing in lung adenocarcinoma (LUCA) on survival benefit: The Lung Cancer Mutation Consortium II (LCMC II) experience.** *Proc ASCO* 2016;**Abstract 11510**.

Awad MM, Shaw AT. **ALK inhibitors in non-small cell lung cancer: crizotinib and beyond.** *Clin Adv Hematol Oncol* 2014;12(7):429-39.

Borghaei H et al. **Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer.** *N Engl J Med* 2015;373(17):1627-39.

De Castro G et al. **First-line ceritinib versus chemotherapy in patients with ALK-rearranged (ALK+) NSCLC: A randomized, Phase 3 study (ASCEND-4).** *Proc WCLC* 2016;**Abstract PL03.07**.

Drilon A 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.

Gettinger SN et al. **Activity and safety of brigatinib in ALK-rearranged non-small-cell lung cancer and other malignancies: A single-arm, open-label, phase 1/2 trial.** *Lancet Oncol* 2016;17(12):1683-96.

Goss G et al. **MA16.11 — CNS response to osimertinib in patients with T790M-positive advanced NSCLC: Pooled data from two Phase II trials.** *Proc WCLC* 2016;**Abstract MA16.11**.

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.

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

Kim D-W et al. **Brigatinib (BRG) in patients (pts) with crizotinib (CRZ)-refractory ALK+ non-small cell lung cancer (NSCLC): First report of efficacy and safety from a pivotal randomized phase (ph) 2 trial (ALTA).** *Proc ASCO* 2016;**Abstract 9007**.

Kim YH et al. **Alectinib (ALC) versus crizotinib (CRZ) in ALK-positive non-small cell lung cancer (ALK+ NSCLC): Primary results from Phase III study (J-ALEX).** *Proc WCLC* 2016;**Abstract MA07.03**.

Kodama T et al. **Alectinib shows potent antitumor activity against RET-rearranged non-small cell lung cancer.** *Mol Cancer Ther* 2014;13(12):2910-8.

Kwak EL et al. **Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer.** *N Engl J Med* 2010;363(18):1693-703.

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.

Mok TS et al. **Osimertinib or platinum-pemetrexed in EGFR T790M-positive lung cancer.** *N Engl J Med* 2017;376(7):629-40.

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**.

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**.

Select Publications

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;34(28):3375-82.

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.

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.

Reungwetwattana T et al. **The race to target MET exon 14 skipping alterations in non-small cell lung cancer: The why, the how, the who, the unknown, and the inevitable.** *Lung Cancer* 2017;103:27-37.

Shaw AT et al. **Crizotinib in advanced ROS1-rearranged non-small cell lung cancer (NSCLC): Updated results from PROFILE 1001.** *Proc ESMO* 2016;**Abstract 1206PD**.

Solomon BJ et al. **Intracranial efficacy of crizotinib versus chemotherapy in patients with advanced ALK-positive non-small-cell lung cancer: Results from PROFILE 1014.** *J Clin Oncol* 2016;34(24):2858-65.

Solomon BJ et al. **Safety and efficacy of lorlatinib (PF-06463922) from the dose-escalation component of a study in patients with advanced ALK+ or ROS1+ non-small cell lung cancer (NSCLC).** *Proc ASCO* 2016;**Abstract 9009**.

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 (pts) with leptomeningeal (LM) disease from non-small cell lung cancer (NSCLC): Updated results from BLOOM, a phase I study.** *Proc ASCO* 2016;**Abstract 9002**.