Beyond the Guidelines

Clinical Investigators Provide Their Perspectives on Current Treatment Strategies and Ongoing Research in the Management of Non-Small Cell Lung Cancer without Targetable Tumor Mutations

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 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. Current therapeutic management of NSCLC is dependent on tumor stage and histology at the time of initial diagnosis and prior treatment exposure, patient performance status and sites of metastasis for those with disease recurrence or de novo Stage IV presentation. Over the past 2 years, major clinical trials in advanced NSCLC have witnessed unexpected failures and promising successes. These setbacks and achievements will without doubt be dissected in the upcoming year and will further challenge the collective understanding of the biology and optimal management of this disease. Until then, several consensus- and evidence-based treatment guidelines are currently available and aim to assist clinicians with making lung cancer treatment decisions in the face of this dynamic clinical environment. But despite the existence of these tools, many areas of controversy persist within academic and community settings.

These video proceedings from a CME symposium held in conjunction with the 16th World Conference on Lung Cancer feature discussions with the world's leading researchers with an expertise in the management of lung cancer regarding actual patient cases and the practice patterns of 31 lung cancer clinical investigators who were surveyed in preparation for this event. By delivering the perspectives of experts in the field on clinical research findings and their application to treatment, this program will assist clinicians in the development of up-to-date therapeutic algorithms for NSCLC without targetable tumor mutations.

LEARNING OBJECTIVES

- Develop an evidence-based strategy for the diagnosis and management of Stage I to III NSCLC, considering the potential contributions of systemic and/or local therapeutic modalities.
- Consider age, performance status and other patient- or disease-related factors to guide the selection of induction and maintenance systemic therapy for patients with metastatic NSCLC without an identifiable driver mutation.
- Identify patients with metastatic NSCLC for whom multiplex genomic testing should be recommended to aid in treatment decision-making or to identify actionable mutations for clinical trial participation.
- Assess available research evidence with existing and emerging therapeutic options for patients with advanced squamous cell carcinoma of the lung, and use this information to guide clinical care and protocol opportunities for these individuals.
- Recognize the recent FDA approval of ramucirumab for patients with progressive, metastatic NSCLC, and discern how this agent can be optimally integrated into clinical practice for patients with squamous and nonsquamous disease.

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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

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Select Publications

Heather Wakelee, MD

Cabillic F et al. **Parallel FISH and immunohistochemical studies of ALK status in 3244 non-small-cell lung cancers reveal major discordances.** *J Thorac Oncol* 2014;9(3):295-306.

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**.

Hirsch FR et al. **The tissue is the issue: Personalized medicine for non-small cell lung cancer.** *Clin Cancer Res* 2010;16(20):4909-11.

Paik PK et al. **Response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping.** *Cancer Discov* 2015;5(8):842-9.

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**.

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

Savic S et al. **Screening for ALK in non-small cell lung carcinomas: 5A4 and D5F3 antibodies perform equally well, but combined use with FISH is recommended.** *Lung Cancer* 2015;89(2):104-9.

Sequist LV et al. **Efficacy of rociletinib (CO-1686) in plasma-genotyped T790M-positive non-small cell lung cancer (NSCLC) patients (pts).** *Proc ASCO* 2015;**Abstract 8001**.

Sholl LM et al. **Multi-institutional oncogenic driver mutation analysis in lung adenocarcinoma: The lung cancer mutation consortium experience.** *J Thorac Oncol* 2015;10(5):768-77.

Wu Y et al. **Can EGFR mutations in plasma or serum be predictive markers of non-small-cell lung cancer? A meta-analysis.** *Lung Cancer* 2015;88(3):246-53.

Yu HA et al. **Analysis of tumor specimens at the time of acquired resistance to EGFR-TKI therapy in 155 patients with EGFR-mutant lung cancers.** *Clin Cancer Res* 2013;19(8):2240-7.

Martin Reck, MD, PhD

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

Besse B et al. **2nd ESMO Consensus Conference on Lung Cancer: Non-small-cell lung cancer first-line/second and further lines of treatment in advanced disease.** *Ann Oncol* 2014;25(8):1475-84.

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.

Ellis LM et al. **American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes.** *J Clin Oncol* 2014;32(12):1277-80.

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.

Reck M et al. **Metastatic non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up.** *Ann Oncol* 2014;25(Suppl 3):iii27-39.

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.

Thatcher N et al. **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.

Select Publications

Corey J Langer, MD

Barlesi F et al. **Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089).** *J Clin Oncol* 2013;31(24):3004-11.

Langer CJ et al. **Isolating the role of bevacizumab in elderly patients with previously untreated nonsquamous non-small cell lung cancer: Secondary analyses of the ECOG 4599 and PointBreak trials.** *Am J Clin Oncol* 2015;[Epub ahead of print].

Niho S et al. **Randomized phase II study of first-line carboplatin-paclitaxel with or without bevacizumab in Japanese patients with advanced non-squamous non-small-cell lung cancer.** *Lung Cancer* 2012;76(3):362-7.

Patel JD et al. **PointBreak: A randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer.** *J Clin Oncol* 2013;31(34):4349-57.

Randomized phase III study of maintenance therapy with bevacizumab, pemetrexed, or a combination of bevacizumab and pemetrexed following carboplatin, paclitaxel and bevacizumab for advanced non-squamous NSCLC. NCT01107626

Reck M et al. **Overall survival with cisplatin-gemcitabine and bevacizumab or placebo as first-line therapy for nonsquamous non-small-cell lung cancer: Results from a randomised phase III trial (AVAiL).** *Ann Oncol* 2010;21(9):1804-9.

Reck M et al. **Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil.** *J Clin Oncol* 2009;27(8):1227-34.

Sandler AB et al. **Clinical patterns and outcomes for the bevacizumab maintenance population in the ECOG E4599 study of patients with advanced non-small cell lung cancer (NSCLC): Results of an exploratory analysis.** *Proc IASLC* 2011;**Abstract P3.216**.

Sandler A et al. **Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.** *N Engl J Med* 2006;355(24):2542-50.

Zinner RG et al. **PRONOUNCE: Randomized, open-label, phase III study of first-line pemetrexed + carboplatin followed by maintenance pemetrexed versus paclitaxel + carboplatin + bevacizumab followed by maintenance bevacizumab in patients with advanced nonsquamous non-small-cell lung cancer.** *J Thorac Oncol* 2015;10(1):134-42.

John V Heymach, MD, PhD

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 phase III randomized trial of adjuvant chemotherapy with or without bevacizumab for patients with completely resected stage IB (≥ 4 cm) – IIIA non-small cell lung cancer (NSCLC). NCT00324805

Arriagada R et al. **Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer.** *N Engl J Med* 2004;350(4):351-60.

Bradley JD et al. **Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): A randomised, two-by-two factorial phase 3 study.** *Lancet Oncol* 2015;16(2):187-99.

DETERRED: PD-L1 blockade to evaluate the safety of lung cancer therapy using carboplatin, paclitaxel, and radiation combined with MPDL3280A. NCT02525757

Douillard JY et al. **Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): A randomised controlled trial.** *Lancet Oncol* 2006;7(9):719-27.

Gandara DR et al. **Consolidation docetaxel after concurrent chemoradiotherapy in Stage IIIB non-small-cell lung cancer: Phase II Southwest Oncology Group study S9504.** *J Clin Oncol* 2003;21(10):2004-10.

Kreuter M et al. **Randomized phase 2 trial on refinement of early-stage NSCLC adjuvant chemotherapy with cisplatin and pemetrexed versus cisplatin and vinorelbine: The TREAT study.** *Ann Oncol* 2013;24(4):986-92.

Pignon JP et al. **Lung adjuvant cisplatin evaluation: A pooled analysis by the LACE Collaborative Group.** *J Clin Oncol* 2008;26(21):3552-9.

Select Publications

PROCLAIM: Phase 3 study of pemetrexed, cisplatin, and radiotherapy followed by consolidation pemetrexed versus etoposide, cisplatin, and radiotherapy followed by consolidation cytotoxic chemotherapy of choice in patients with unresectable, locally advanced, stage III non-small cell lung cancer other than predominantly squamous cell histology. NCT00686959

Strauss GM et al. **Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study groups.** *J Clin Oncol* 2008;26(31):5043-51.

Winton T et al. **Vinorelbine plus cisplatin vs observation in resected non-small-cell lung cancer.** *N Engl J Med* 2005;352(25):2589-97.

Wislez M et al. **Customized adjuvant phase II trial in patients with non-small-cell lung cancer: IFCT-0801 TASTE.** *J Clin Oncol* 2014;32(12):1256-61.