Cases from the Community

Clinical Investigators Provide Their Perspectives on Emerging Research and Actual Patients with 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 14% of all new cancer cases in the United States and the most cancer-related deaths among both men and women. In the year 2018, it is estimated that approximately 234,030 individuals will be diagnosed and 154,050 will die from the disease. Of importance, 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, many have renewed optimism 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. Over the past several years major clinical trials in NSCLC have witnessed a host of promising successes, many of which are already being operationalized in clinical practice. Even so, these achievements will doubtlessly continue to be dissected in the upcoming years and will further challenge the collective understanding of the biology and optimal management of this disease.

These proceedings from a CME symposium during the 2018 ASCO Annual Meeting explore the most significant therapeutic advances in the field of NSCLC by using the perspectives of leading lung cancer experts on challenging cases and questions submitted by clinicians in the community to frame a relevant discussion of how this information has aided in the refinement of current routine clinical practice and ongoing research. This CME activity will help medical oncologists and other allied healthcare professionals find answers to the individualized questions and concerns that they frequently encounter and in turn provide high-quality cancer care.

LEARNING OBJECTIVES

- Appreciate available Phase III data documenting the benefit of sequential anti-PD-L1 therapy after completion of chemoradiation therapy for Stage III NSCLC, and consider the role of durvalumab for appropriate patients.
- Recognize available and emerging research information validating the utility of diagnostic assays designed to measure EGFR, ALK, ROS1, BRAF and PD-L1 status, assess which testing platforms should be used and appropriately employ the results of these assessments to individualize first- and later-line therapy for patients with metastatic NSCLC.
- Recall the results from the Phase III FLAURA trial and consider how, if at all, these findings and the subsequent FDA approval of osimertinib as first-line therapy affect current or future therapy for patients with EGFR mutations.
- Communicate the efficacy and safety of approved and investigational ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK mutation testing.
- Review published research documenting the safety and efficacy of anti-PD-1/PD-L1 antibodies used as monotherapy or in combination with chemotherapy with or without anti-VEGF therapy for newly diagnosed metastatic NSCLC.
- Consider available Phase III data comparing nivolumab in combination with ipilimumab to chemotherapy as first-line treatment for patients with NSCLC and a high tumor mutational burden.
- Describe ongoing research to assist in the identification of additional biomarkers, tumor characteristics or other clinical features that are indicative of response to immune checkpoint inhibitors in patients with NSCLC.
- Recall the design of ongoing clinical trials evaluating anti-PD-1/PD-L1 antibodies in combination with other immunotherapeutic and systemic therapies for NSCLC, and counsel appropriate patients about availability and participation.

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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 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

Neil Love, MD

Love N et al. **A biomarker-driven algorithm for sequencing of systemic therapy for metastatic NSCLC: A survey of 25 investigators.** *Proc IASLC* 2017;**Abstract PS02.17**.

Geoffrey R Oxnard, MD

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.

Gallant JN et al. **EGFR kinase domain duplication (EGFR-KDD) is a novel oncogenic driver in lung cancer that is clinically responsive to afatinib.** *Cancer Discov* 2015;5(11):1155-63.

Konduri K et al. **EGFR fusions as novel therapeutic targets in lung cancer.** *Cancer Discov* 2016;6(6):601-11.

Lisberg AE et al. **A phase II study of pembrolizumab in EGFR-mutant, PD-L1+, tyrosine kinase inhibitor (TKI) naïve patients with advanced NSCLC.** ASCO 2018;**Abstract 9014**.

Martínez P et al. **Targeted therapy as an alternative to whole-brain radiotherapy in EGFR-mutant or ALK-positive non-small-cell lung cancer with brain metastases.** *JAMA Oncol* 2017;3(9):1274-5.

Midha A et al. **EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: A systematic review and global map by ethnicity (mutMapII).** *Am J Cancer Res* 2015;5(9):2892-911.

Mok TS et al. **CNS response to osimertinib in patients (pts) with T790M-positive advanced NSCLC: Data from a randomized phase III trial (AURA3).** ASCO 2017;**Abstract 9005**.

Mok TS et al; AURA3 Investigators. **Osimertinib or platinum-pemetrexed in EGFR T790M-positive lung cancer.** *N Engl J Med* 2017;376(7):629-40.

Socinski MA et al. **Overall survival (OS) analysis of IMpower150, a randomized ph 3 study of atezolizumab (atezo) + chemotherapy (chemo) ± bevacizumab (bev) vs chemo + bev in 1L nonsquamous (NSQ) NSCLC.** ASCO 2018;**Abstract 9002**.

Soria JC et al; FLAURA Investigators. **Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer.** *N Engl J Med* 2018;378(2):113-25.

Wu YL et al. **Dacomitinib versus gefitinib as first-line treatment for patients with EGFR-mutation-positive non-small-cell lung cancer (ARCHER 1050): A randomised, open-label, phase 3 trial.** *Lancet Oncol* 2017;18(11):1454-66.

Yang J C-H et al. **Osimertinib for patients (pts) with leptomeningeal metastases (LM) from EGFR-mutant non-small cell lung cancer (NSCLC): Updated results from the BLOOM study.** ASCO 2017;**Abstract 2020**.

Alice Shaw, MD, PhD

Camidge DR et al. **Exploratory analysis of brigatinib activity in patients with anaplastic lymphoma kinase-positive non-small-cell lung cancer and brain metastases in two clinical trials.** *J Clin Oncol* 2018;[Epub ahead of print].

Davies H et al. **Mutations of the BRAF gene in human cancer.** *Nature* 2002;417(6892):949-54.

Gainor JF et al. **Molecular mechanisms of resistance to first- and second-generation ALK inhibitors in ALK-rearranged lung cancer.** *Cancer Discov* 2016;6(10):1118-33.

Gilmartin AG et al. **GSK1120212 (JTP-74057) is an inhibitor of MEK activity and activation with favorable pharmacokinetic properties for sustained in vivo pathway inhibition.** *Clin Cancer Res* 2011;17(5):989-1000.

Johnson TW et al. **Discovery of (10R)-7-amino-12-fluoro-2,10,16-trimethyl-15-oxo-10,15,16,17-tetrahydro-2H-8,4-(metheno) pyrazolo[4,3-h][2,5,11]-benzoxadiazacyclotetradecine-3-carbonitrile (PF-06463922), a macrocyclic inhibitor of anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 (ROS1) with preclinical brain exposure and broad-spectrum potency against ALK-resistant mutations.** *J Med Chem* 2014;57(11):4720-44.

Karasarides M et al. **B-RAF is a therapeutic target in melanoma.** *Oncogene* 2004;23(37):6292-8.

Kim DW et al. **Brigatinib in patients with crizotinib-refractory anaplastic lymphoma kinase-positive non-small-cell lung cancer: A randomized, multicenter phase II trial.** *J Clin Oncol* 2017;35(22):2490-8.

Lim SM et al. **Open-label, multicenter, phase II study of ceritinib in patients with non-small-cell lung cancer harboring ROS1 rearrangement.** *J Clin Oncol* 2017;35(23):2613-8.

Long GV et al. **Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma.** *N Engl J Med* 2014;371(20):1877-88.

Select Publications

Mazières J et al. **Crizotinib therapy for advanced lung adenocarcinoma and a ROS1 rearrangement: Results from the EUROS1 cohort.** *J Clin Oncol* 2015;33(9):992-9.

Moro-Sibilot D et al. **Crizotinib in patients with advanced ROS1-rearranged non-small cell lung cancer (NSCLC): Preliminary results of the ACSé phase II trial.** ASCO 2015;**Abstract 8065**.

Platz A et al. **Human cutaneous melanoma; a review of NRAS and BRAF mutation frequencies in relation to histogenetic subclass and body site.** *Mol Oncol* 2008;1(4):395-405.

Shaw AT et al. **Crizotinib in ROS1-rearranged non-small-cell lung cancer.** *N Engl J Med* 2014;371(21):1963-71.

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Antonia SJ et al. **Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer.** *N Engl J Med* 2017;377(20):1919-29.

Aupérin A et al. **Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer.** *J Clin Oncol* 2010;28(13):2181-90.

Aupérin A et al. **Concomitant radio-chemotherapy based on platin compounds in patients with locally advanced non-small cell lung cancer (NSCLC): A meta-analysis of individual data from 1764 patients.** *Ann Oncol* 2006;17(3):473-83.

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.

Daly ME et al. **Clinical trials integrating immunotherapy and radiation for non-small-cell lung cancer.** *J Thorac Oncol* 2015;10(12):1685-93.

Deng L et al. **Irradiation and anti-PD-L1 treatment synergistically promote antitumor immunity in mice.** *J Clin Invest* 2014;124(2):687-95.

Fournel P et al. **Randomized phase III trial of sequential chemoradiotherapy compared with concurrent chemoradiotherapy in locally advanced non-small-cell lung cancer: Groupe Lyon-Saint-Etienne d'Oncologie Thoracique-Groupe Français de Pneumo-Cancérologie NPC 95-01 Study.** *J Clin Oncol* 2005;23(25):5910-7.

Hanna N et al; Hoosier Oncology Group; US Oncology. **Phase III study of cisplatin, etoposide, and concurrent chest radiation with or without consolidation docetaxel in patients with inoperable stage III non-small-cell lung cancer: The Hoosier Oncology Group and U.S. Oncology.** *J Clin Oncol* 2008;26(35):5755-60.

Johnson DH. **Locally advanced, unresectable non-small cell lung cancer: New treatment strategies.** *Chest* 2000;117:123S-6S.

Kaur P, Asea A. **Radiation-induced effects and the immune system in cancer.** *Front Oncol* 2012;2:191.

Kelly K et al. **Phase III trial of maintenance gefitinib or placebo after concurrent chemoradiotherapy and docetaxel consolidation in inoperable stage III non-small-cell lung cancer: SWOG S0023.** *J Clin Oncol* 2008;26(15):2450-6.

Lilenbaum R et al. **A phase II study of induction chemotherapy followed by thoracic radiotherapy and erlotinib in poor risk stage III non-small cell lung cancer: Results of CALGB 30605 (Alliance)/RTOG 0972 (NRG).** *J Thorac Oncol* 2015;10(1):143-7.

Non-Small Cell Lung Cancer Collaborative Group. **Chemotherapy in non-small cell lung cancer: A meta-analysis using updated data on individual patients from 52 randomised clinical trials.** *BMJ* 1995;311(7010):899-909.

Provencio M et al. **Inoperable stage III non-small cell lung cancer: Current treatment and role of vinorelbine.** *J Thorac Dis* 2011;3:197-204.

Scorsetti M et al. **Large volume unresectable locally advanced non-small cell lung cancer: Acute toxicity and initial outcome results with rapid arc.** *Radiat Oncol* 2010;5:94.

Corey J Langer, MD

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

Reck M et al. **Primary PFS and safety analyses of a randomized phase III study of carboplatin + paclitaxel +/– bevacizumab, with or without atezolizumab in 1L non-squamous metastatic NSCLC (IMpower150).** *Proc ESMO Immuno-Oncology Congress* 2017;**Abstract LBA1_PR**.

Select Publications

Socinski M et al. **Overall survival (OS) analysis of IMpower150, a randomized Ph 3 study of atezolizumab (atezo) + chemotherapy (chemo) ± bevacizumab (bev) vs chemo + bev in 1L nonsquamous (NSQ) NSCLC.** ASCO 2018;**Abstract 9002**.

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Carbone DP et al; CheckMate 026 Investigators. **First-line nivolumab in stage IV or recurrent non-small-cell lung cancer.** *N Engl J Med* 2017;376(25):2415-26.

Hellmann MD et al. **Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden.** *N Engl J Med* 2018;378(22):2093-104.

Hellmann MD et al. **Tumor mutational burden and efficacy of nivolumab monotherapy and in combination with ipilimumab in small-cell lung cancer.** *Cancer Cell* 2018;33(5):853-61.

Jordan EJ et al. **Prospective comprehensive molecular characterization of lung adenocarcinomas for efficient patient matching to approved and emerging therapies.** *Cancer Disc* 2017;7(6):596-609.

Kowanetz M et al. **Tumor mutation load assessed by FoundationOne (FM1) is associated with improved efficacy of atezolizumab (atezo) in patients with advanced NSCLC.** *Proc ESMO* 2016;**Abstract77P**.

Salem ME et al. **Landscape of tumor mutation load, mismatch repair deficiency, and PD-L1 expression in a large patient cohort of gastrointestinal cancers.** *Mol Cancer Res* 2018;16(5):805-12.