BEYOND THE GUIDELINES

Clinical Investigator Perspectives on the Management of Lung Cancer

CME Information

TARGET AUDIENCE

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

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 2019, it is estimated that approximately 228,150 individuals will be diagnosed and 142,670 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 lung cancer 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.

Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making management decisions in this dynamic clinical and research environment. However, in situations where multiple acceptable therapeutic options exist, such guidelines may not be particularly helpful at the time of decision-making. By exploring the perspectives of leading investigators regarding a number of clinical scenarios and reviewing key data sets, these proceedings from a CME symposium during the 2019 ASCO Annual Meeting will assist medical oncologists and other allied healthcare professionals in the development of evidence-based strategies for the treatment of lung cancer.

LEARNING OBJECTIVES

- Appraise the recent FDA approval of anti-PD-L1 antibody consolidation therapy for patients with unresectable Stage III non-small cell lung cancer (NSCLC) who have not experienced disease progression after standard platinum-based chemotherapy concurrent with radiation therapy, and discern how this strategy can be appropriately and safely integrated into routine clinical practice.
- Review recent FDA approvals and other therapeutic advances related to the use of anti-PD-1/PD-L1 antibodies as monotherapy or in combination with chemotherapy or chemobiologic therapy for newly diagnosed metastatic NSCLC.
- Consider emerging research data and available guidelines informing the use of immune checkpoint inhibitors for patients with advanced small cell lung cancer (SCLC).
- Recall the design of ongoing clinical trials evaluating anti-PD-1/PD-L1 antibodies in combination with other systemic therapies for NSCLC and SCLC, and counsel appropriate patients about availability and participation.
- Review published research data documenting the safety and efficacy of EGFR tyrosine kinase inhibitors for metastatic NSCLC with an EGFR tumor mutation, and discern how this information should be applied outside of a research setting.
- Communicate the efficacy and safety of approved and investigational ALK inhibitors to appropriate patients with NSCLC.
- Assess other oncogenic pathways mediating tumor growth in unique patient subgroups, and recall emerging data with commercially available and experimental agents exploiting these targets.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 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

Gregory J Riely, MD, PhD

Le X et al. **Landscape of EGFR-dependent and -independent resistance mechanisms to osimertinib and continuation therapy beyond progression in EGFR-mutant NSCLC.** *Clin Cancer Res* 2018;24(24):6195-203.

Mok T et al. **Dacomitinib (daco) versus gefitinib (gef) for first-line treatment of advanced NSCLC (ARCHER 1050): Final overall survival (OS) analysis.** *Proc ASCO* 2018;**Abstract 9004**.

Mok TS et al. **Improvement in overall survival in a randomized study that compared dacomitinib with gefitinib in patients with advanced non-small-cell lung cancer and EGFR-activating mutations.** *J Clin Oncol* 2018;36(22):2244-50.

Piotrowska Z et al. **Landscape of acquired resistance to osimertinib in EGFR-mutant NSCLC and clinical validation of combined EGFR and RET inhibition with osimertinib and BLU-667 for acquired RET fusion.** *Cancer Discov* 2018;8(12):1529-39.

Piotrowska Z et al. **Heterogeneity underlies the emergence of EGFRT790 wild-type clones following treatment of T790M-positive cancers with a third-generation EGFR inhibitor.** *Cancer Discov* 2015;5(7):713-22.

Reungwetwattana T et al. **CNS response to osimertinib versus standard epidermal growth factor receptor tyrosine kinase inhibitors in patients with untreated EGFR-mutated advanced non-small-cell lung cancer.** *J Clin Oncol* 2018;[Epub ahead of print].

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

Thress KS et al. **Acquired EGFR C797S mutation mediates resistance to AZD9291 in non-small cell lung cancer harboring EGFR T790M.** *Nat Med* 2015;21(6):560-2.

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.

Yu HA et al. **Acquired resistance of EGFR-mutant lung cancer to a T790M-specific EGFR inhibitor: Emergence of a third mutation (C797S) in the EGFR tyrosine kinase domain.** *JAMA Oncol* 2015;1(7):982-4.

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.

D Ross Camidge, MD, PhD

Besse B et al. **Lorlatinib in patients (Pts) with previously treated ALK+ advanced non-small cell lung cancer (NSCLC): Updated efficacy and safety.** *Proc ASCO* 2018;**Abstract 9032**.

Camidge DR et al. **Brigatinib versus crizotinib in ALK-positive non-small-cell lung cancer.** *N Engl J Med* 2018;379(21):2027-39.

Camidge DR et al. **Updated efficacy and safety data from the global phase III ALEX study of alectinib (ALC) vs crizotinib (CZ) in untreated advanced ALK+ NSCLC.** *Proc ASCO* 2018;**Abstract 9043**.

Crino L et al. **Multicenter phase II study of whole-body and intracranial activity with ceritinib in patients with ALK-rearranged non-small-cell lung cancer previously treated with chemotherapy and crizotinib: Results from ASCEND-2.** *J Clin Oncol* 2016;34(24):2866-73.

Descourt R et al. **Brigatinib in pretreated patients with ALK-positive advanced NSCLC.** *Proc ASCO* 2019;**Abstract 9045**.

Doebele RC et al. **Efficacy and safety of entrectinib in locally advanced or metastatic ROS1 fusion-positive non-small cell lung cancer (NSCLC).** *Proc WCLC* 2018;**Abstract OA02.01**.

Drilon A et al. **Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children.** *N Engl J Med* 2018;378(8):731-9.

Gadgeel S et al. **Alectinib vs crizotinib in treatment-naïve ALK+ NSCLC: CNS efficacy results from the ALEX study.** *Proc ESMO* 2017;**Abstract 1298O_PR**.

Hida T et al. **Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): An open-label, randomised phase 3 trial.** *Lancet* 2017;390(10089):29-39.

Horn L et al. **Ensartinib (X-396) in ALK-positive non-small cell lung cancer: Results from a first-in-human phase I/II, multicenter study.** *Clin Cancer Res* 2018;24(12):2771-9.

Ou SHI et al. **Alectinib in crizotinib-refractory ALK-rearranged non-small-cell lung cancer: A phase II global study.** *J Clin Oncol* 2016;34(7):661-8.

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Peters S et al; ALEX Trial Investigators. **Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer.** *N Engl J Med* 2017;377(9):829-83.

Shaw AT et al. **Efficacy of lorlatinib in patients (pts) with advanced ALK-positive non-small cell lung cancer (NSCLC) and ALK kinase domain mutations.** *Proc AACR* 2018;**Abstract CT044**.

Shaw AT et al. **Alectinib in ALK-positive, crizotinib-resistant, non-small-cell lung cancer: A single-group, multicentre, phase 2 trial.** *Lancet Oncol* 2016;17(2):234-42.

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. **First-line crizotinib versus chemotherapy in ALK-positive lung cancer.** *N Engl J Med* 2014;371(23):2167-77.

Soria JC et al. **First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): A randomised, open-label, phase 3 study.** *Lancet* 2017;389(10072):917-29.

Stinchcombe T et al. **Preliminary results of single arm phase 2 trial of brigatinib in patients (pts) with progression disease (PD) after next-generation (NG) anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitors (TKIs) in *ALK*+ non-small cell lung cancer (NSCLC).** *Proc ASCO* 2019;**Abstract 9027**.

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Antonia SJ et al. **Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): A multicentre, open-label, phase 1/2 trial.** *Lancet Oncol* 2016;17(7):883-95.

Chung HC et al. **Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158.** *Proc ASCO* 2018;**Abstract 8506**.

Hellmann MD et al. **Genomic features of response to combination immunotherapy in patients with advanced non-small-cell lung cancer.** *Cancer Cell* 2018;33(5):843-52.e4.

Hellmann MD et al. **Nivolumab (nivo) ± ipilimumab (ipi) in advanced small-cell lung cancer (SCLC): First report of a randomized expansion cohort from CheckMate 032.** *Proc ASCO* 2017;**Abstract 8503**.

Horn L et al; IMpower133 Study Group. **First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer.** *N Engl J Med* 2018;379(23):2220-9.

Liu S et al. **IMpower 133: Primary PFS, OS and safety in a PH1/3 study of 1L atezolizumab + carboplatin + etoposide in extensive-stage SCLC.** *Proc WCLC* 2018;**Abstract PL02.07**.

Owonikoko TK et al. **Nivolumab (nivo) plus ipilimumab (ipi), nivo, or placebo (pbo) as maintenance therapy in patients (pts) with extensive disease small cell lung cancer (ED-SCLC) after first-line (1L) platinum-based chemotherapy (chemo): Results from the double-blind, randomized phase III CheckMate 451 study.** *Proc ELCC* 2019;**Abstract LBA1_PR**.

Ready N et al. **Third-line nivolumab monotherapy in recurrent SCLC: CheckMate 032.** *J Thorac Oncol* 2019;14(2):237-44.

David R Spigel, MD

Antonia SJ et al. **Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC.** *N Engl J Med* 2018;379(24):2342-50.

Chacon JA et al. **The impact of chemotherapy, radiation and epigenetic modifiers in cancer cell expression of immune inhibitory and stimulatory molecules and anti-tumor efficacy.** *Vaccines (Basel)* 2016;4(4).

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

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Durm G et al. **Updated results of a phase II trial of concurrent chemoradiation with consolidation pembrolizumab in patients with unresectable stage III NSCLC.** *J Thorac Oncol* 2018;13(10):S321.

Forde P et al. **Neoadjuvant PD-1 blockade in resectable lung cancer.** *N Engl J Med* 2018;378(21):1976-86.

Formenti SC, Demaria S. **Combining radiotherapy and cancer immunotherapy: A paradigm shift.** *J Natl Cancer Inst* 2013;105(4):256-65.

Select Publications

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Barlesi F et al. **IMpower132: Efficacy of atezolizumab (atezo) + carboplatin (carbo)/cisplatin (cis) + pemetrexed (pem) as 1L treatment in key subgroups with stage IV non-squamous non-small cell lung cancer (NSCLC).** *Proc ESMO* 2018;**Abstract LBA54**.

Brahmer J et al. **Updated analysis of KEYNOTE-024: Pembrolizumab vs platinum-based chemotherapy for advanced NSCLC with PD-L1 TPS ≥50%.** *Proc WCLC* 2017;**Abstract OA 17.06**.

Cappuzzo F et al. **IMpower130: Progression-free survival (PFS) and safety analysis from a randomised phase 3 study of carboplatin + *nab*-paclitaxel (CnP) with or without atezolizumab (atezo) as first-line (1L) therapy in advanced non-squamous NSCLC.** *Proc ESMO* 2018;**Abstract LBA53**.

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

Gandhi L et al. **KEYNOTE-189: Randomized, double-blind, phase 3 study of pembrolizumab (pembro) or placebo plus pemetrexed (pem) and platinum as first-line therapy for metastatic NSCLC.** *Proc AACR* 2018;**Abstract CT075**.

Jotte RM et al. **IMpower131: Primary PFS and safety analysis of a randomized phase III study of atezolizumab + carboplatin + paclitaxel or *nab*-paclitaxel vs carboplatin + *nab*-paclitaxel as 1L therapy in advanced squamous NSCLC.** *Proc ASCO* 2018;**Abstract LBA9000**.

Lopes G et al. **Pembrolizumab (pembro) versus platinum-based chemotherapy (chemo) as first-line therapy for advanced/metastatic NSCLC with a PD-L1 tumor proportion score (TPS) ≥ 1%: Open-label, phase 3 KEYNOTE-042 study.** *Proc ASCO* 2018;**Abstract LBA4**.

Melero I et al. **Evolving synergistic combinations of targeted immunotherapies to combat cancer.** *Nat Rev Cancer* 2015;15(8):457-72.

Mok TS et al; KEYNOTE-042 Investigators. **Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): A randomised, open-label, controlled, phase 3 trial.** *Lancet* 2019;393(10183):1819-30.

Paz-Ares LG et al. **Results from a second-line (2L) NSCLC cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1.** *Proc ASCO* 2018;**Abstract 9017**.

Reck M et al. **Pembrolizumab versus chemotherapy for PD-L1–positive non–small-cell lung cancer.** *N Engl J Med* 2016;375:1823-33.

Socinski MA et al; IMpower150 Study Group. **Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC.** *N Engl J Med* 2018;378(24):2288-301.