

Cases from the Community

Clinical Investigators Provide Their Perspectives on Emerging Research and Actual Patients with Non-Small Cell Lung Cancer

A Special Audio Supplement

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 effects 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. Despite 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, hope is renewed that these patterns have started to change as recent research advances have led to an explosion in lung cancer genetic and biologic knowledge among scientists and clinicians. Over the past several years, major clinical trials in NSCLC have recorded a host of promising successes, many of which are already being applied in clinical practice. Even so, these achievements will doubtless continue to be dissected in the upcoming years and will further challenge the collective understanding of the biology and optimal management of this disease.

This CME program was developed from the proceedings of a satellite symposium held during the 2018 ASCO Annual Meeting. It explores 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 community oncologists to frame a discussion of how this information has aided in the refinement of current clinical practice and ongoing research. This activity will help medical oncologists and other allied healthcare professionals to find answers to the individualized questions and concerns they frequently encounter and to in turn provide high-quality cancer care.

LEARNING OBJECTIVES

- Use patient and disease variables in addition to published research data to guide the selection of therapy for patients with EGFR, ALK, ROS1 and BRAF mutation-positive NSCLC.

- Recall available Phase III data documenting the benefit of sequential anti-PD-L1 therapy after completion of chemoradiation therapy for patients with Stage III NSCLC, and consider the role of durvalumab for appropriate patients.
- Appreciate the recent FDA approval of osimertinib as first-line therapy for patients with EGFR mutation-positive NSCLC, and integrate osimertinib into the clinical management of this disease.
- Appraise emerging research data evaluating anti-PD-1/PD-L1 antibodies as monotherapy or in combination with other systemic approaches for patients with metastatic NSCLC.
- Educate patients about the side effects associated with immune checkpoint inhibitors, and provide preventive strategies to reduce or ameliorate these toxicities.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at ResearchToPractice.com/Privacy-Policy for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of an audio component. To receive credit, the participant should review the CME information, listen to the MP3s, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/ASCOLung18/Audio/CME.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed 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 relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

Matthew D Hellmann, MD

Medical Oncologist
Memorial Sloan Kettering Cancer Center
New York, New York

Consulting Agreements: AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech, Janssen Biotech Inc, Merck, Novartis.

Corey J Langer, MD

Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Vice Chair, Radiation Therapy Oncology Group
Philadelphia, Pennsylvania

Advisory Committee: Abbott Laboratories, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Genentech, Lilly, Merck, Pfizer Inc, Roche Laboratories Inc, Takeda Oncology; **Consulting Agreements:** AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Eisai Inc, Genentech, Lilly, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc, Takeda Oncology; **Contracted Research:** Advantagene Inc, Ariad Pharmaceuticals Inc, GlaxoSmithKline,

Inovio Pharmaceuticals Inc, Merck, Takeda Oncology; **Data and Safety Monitoring Board:** Amgen Inc.

Geoffrey R Oxnard, MD

Lowe Center for Thoracic Oncology
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Consulting Agreements: AstraZeneca Pharmaceuticals LP, DropWorks CEI, GRAIL Inc, Guardant Health Inc, Ignyta Inc, Inivata, Loxo Oncology Inc.

Martin Reck, MD, PhD

Head of Department of Thoracic Oncology
Head of Clinical Trial Department
LungenClinic Grosshansdorf
Grosshansdorf, Germany

Consulting Agreements and Contracted Research: Abbott Laboratories, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, EMD Serono Inc, Lilly, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc; **Speakers Bureau:** Abbott Laboratories, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, EMD Serono Inc, Lilly, Merck, Pfizer Inc, Roche Laboratories Inc.

Alice Shaw, MD, PhD

Professor of Medicine
Harvard Medical School
Center for Thoracic Cancers
Massachusetts General Hospital
Boston, Massachusetts

Advisory Committee: Blueprint Medicines; **Consulting Agreements:** Ariad Pharmaceuticals Inc, Blueprint Medicines, Daiichi Sankyo Inc, EMD Serono Inc, Foundation Medicine, Genentech, Ignyta Inc, KSQ Therapeutics, Loxo Oncology Inc, Natera Inc, Novartis, Pfizer Inc, Roche Laboratories Inc, Takeda Oncology.

MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation

Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

RESEARCH TO PRACTICE CME PLANNING COMMITTEE MEMBERS, STAFF AND REVIEWERS

— Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Foundation Medicine, Genentech, Merck and Takeda Oncology.

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

Release date: July 2018

Expiration date: July 2019

Select Publications

- 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.
- 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].
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- Johnson DH. **Locally advanced, unresectable non-small cell lung cancer: New treatment strategies.** *Chest* 2000;117(4 Suppl 1):123-6.
- Jordan EJ et al. **Prospective comprehensive molecular characterization of lung adenocarcinomas for efficient patient matching to approved and emerging therapies.** *Cancer Discov* 2017;7(6):596-609.
- Karasarides M et al. **BRAF 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.
- Konduri K et al. **EGFR fusions as novel therapeutic targets in lung cancer.** *Cancer Discov* 2016;6(6):601-11.
- 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.
- Lisberg AE et al. **A phase II study of pembrolizumab in EGFR-mutant, PD-L1+, tyrosine kinase inhibitor (TKI) naïve patients with advanced NSCLC.** *Proc ASCO* 2018;Abstract 9014.
- Long GV et al. **Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma.** *N Engl J Med* 2014;371(20):1877-88.
- 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.
- 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.

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.
- 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).** *Proc 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.
- Peters S et al. **Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer.** *N Engl J Med* 2017(9);377:829-38.
- Planchard D et al. **Dabrafenib plus trametinib in patients with previously untreated BRAF^{V600E}-mutant metastatic non-small-cell lung cancer: An open-label, phase 2 trial.** *Lancet Oncol* 2017;18(10):1307-16.
- 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.
- 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.
- Shaw AT et al. **Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): A randomised, controlled, open-label, phase 3 trial.** *Lancet Oncol* 2017;18(7):874-86.
- Shaw AT et al. **Crizotinib in ROS1-rearranged non-small-cell lung cancer.** *N Engl J Med* 2014;371(21):1963-71.
- 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.** *Proc 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.
- 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.
- 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.** *Proc ASCO* 2017;Abstract 2020.