Consensus or Controversy?

Clinical Investigators Provide Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Lung Cancer

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

The past several years have seen an explosion in the emergence of new potential therapies that leverage the natural ability of the human body to attack and treat cancer. Known as immune-mediated therapies or cancer immunotherapies, these promising treatments are taking center stage at medical conferences and generating excitement all over the world. Perhaps the most exciting arena in this regard has been the development and assessment of a class of checkpoint inhibitors that inhibit PD-1 or PD-L1. To date, studies with these agents have demonstrated a high degree of activity with limited toxicity in the metastatic and, more recently, locally advanced settings. The availability of these novel compounds has rapidly upended traditional therapeutic sequencing and caused both shifts and rifts in clinical management algorithms, and a number of controversies and questions remain with regard to the current application of these agents in clinical practice.

These video proceedings from a CME symposium held during the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium feature discussions with leading researchers with an expertise in lung cancer. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical, radiation and thoracic oncologists and other healthcare providers with the optimal incorporation of immune checkpoint inhibitors in lung cancer.

LEARNING OBJECTIVES

- Compare and contrast the mechanisms of action, efficacy and safety/toxicity of approved and investigational anti-PD-1/PD-L1 antibodies for the treatment of non-small cell lung cancer (NSCLC) to determine the current and/or potential utility of each in clinical practice.
- Review published research data documenting the safety and efficacy of anti-PD-1 antibodies as monotherapy or in combination with chemotherapy for newly diagnosed metastatic NSCLC.
- Appraise emerging research data documenting the benefits and risks of sequential anti-PD-L1 antibody therapy for patients with unresectable Stage III NSCLC who have not experienced disease progression after standard platinum-based chemotherapy concurrent with radiation therapy.
- Recognize immune-related adverse events and other common side effects associated with approved and developmental immune checkpoint inhibitors, and offer supportive management strategies to minimize and/or manage these toxicities.
- Recall the design of ongoing clinical trials evaluating novel immunotherapeutic approaches alone or in combination with other systemic therapies for NSCLC, and counsel appropriate patients about availability and participation.
- Describe the biologic rationale and eligibility criteria for late-stage clinical trials evaluating novel applications of immune checkpoint inhibitors alone or in combination with other approaches (eg, anti-PD-1/PD-L1 antibodies in combination with other checkpoint inhibitors, radiation therapy, et cetera) for small cell lung cancer, and, where applicable, refer eligible patients for participation or other expanded access programs.

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

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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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No relevant conflicts of interest to disclose.

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MODERATOR — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, 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 BioOncology, 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.

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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

Neil Love, MD

Goodman A et al. **Analysis of over 100,000 patients with cancer for *CD274 (PD-L1)* amplification: Implications for treatment with immune checkpoint blockade.** *Proc ASCO-SITC* 2018;**Abstract 47**.

David R Spigel, MD

Ahn JS et al. **Multinational randomized phase III trial with or without consolidation chemotherapy using docetaxel and cisplatin after concurrent chemoradiation in inoperable stage III non-small-cell lung cancer: KCSG-LU05-04.** *J Clin Oncol* 2015;33(24):2660-6.

Antonia SJ et al. **Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer.** *N Engl J Med* 2016;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.

Meza R et al. **Lung cancer incidence trends by gender, race and histology in the United States, 1973-2010.** *PLoS One* 2015;10(3):e0121323.

Paz-Ares L et al. **PACIFIC: A double-blind, placebo-controlled phase III study of durvalumab after chemoradiation therapy (CRT) in patients with stage III, locally advanced, unresectable NSCLC.** *Proc ESMO* 2017;**Abstract LBA1_PR**.

Senan S et al. **PROCLAIM: Randomized phase III trial of pemetrexed-cisplatin or etoposide-cisplatin plus thoracic radiation therapy followed by consolidation chemotherapy in locally advanced nonsquamous non-small-cell lung cancer.** *J Clin Oncol* 2016;34(9):953-62.

Heather Wakelee, MD

Johnston DB et al. **Immune checkpoint inhibitors in challenging populations.** *Cancer* 2017;123(11):1904-11.

Kanz BA et al. **Safety and efficacy of anti-PD-1 in patients with baseline cardiac, renal, or hepatic dysfunction.** *J Immunother Cancer* 2016;4:60.

Khan SA et al. **How does autoimmune disease impact treatment and outcomes among patients with lung cancer? A national SEER-Medicare analysis.** *Lung Cancer* 2018;115:97-102.

Kittai AS et al. **Immune checkpoint inhibitors in organ transplant patients.** *J Immunother* 2017;40(7):277-81.

Kuo JC et al. **Immune checkpoint inhibitor therapy in a liver transplant recipient with a rare subtype of melanoma: A case report and literature review**. *Melanoma Res* 2018;28(1):61-4.

Kumar V et al. **Current diagnosis and management of immune related adverse events (irAEs) induced by immune checkpoint inhibitor therapy.** *Front Pharmacol* 2017;8:49.

Kwatra V et al. **Pembrolizumab for metastatic melanoma in a renal allograft recipient with subsequent graft rejection and treatment response failure: A case report.** *J Med Case Rep* 2017;11(1):73.

Owonikoko TK et al. **Cardiac allograft rejection as a complication of PD-1 checkpoint blockade for cancer immunotherapy: A case report.** *Cancer Immunol Immunother* 2017;66(1):45-50.

Santini FC et al. **Safety of retreatment with immunotherapy after immune-related toxicity in patients with lung cancers treated with anti-PD(L)-1 therapy.** *Proc ASCO* 2017;**Abstract 9012**.

Weber JS et al. **Toxicities of immunotherapy for the practitioner.** *J Clin Oncol* 2015;33(18):2092-9.

Weber JS et al. **Management of immune-related adverse events and kinetics of response with ipilimumab.** *J Clin Oncol* 2012;30(21):2691-7.

Winkler JK et al. **Safe administration of an anti-PD-1 antibody to kidney-transplant patients: 2 clinical cases and review of the literature.** *J Immunother* 2017;40(9):341-4.

Corey J Langer, MD

A randomized, double-blind, phase III study of platinum+pemetrexed chemotherapy with or without pembrolizumab (MK-3475) in first line metastatic non-squamous non-small cell lung cancer subjects (KEYNOTE-189). NCT02578680

Borghaei H et al. **Updated results from KEYNOTE-021 cohort G: A randomized, phase 2 study of pemetrexed and carboplatin (PC) with or without pembrolizumab (pembro) as first-line therapy for advanced nonsquamous NSCLC.** *Proc ESMO* 2017;**Abstract LBA49**.

Select Publications

Kowanetz M et al. **Pre-existing immunity measured by Teff gene expression in tumor tissue is associated with atezolizumab efficacy in NSCLC.** *Proc IASLC* 2017;**Abstract MA 05.09**.

Langer CJ. **Pemetrexed-carboplatin plus pembrolizumab as first-line therapy for advanced nonsquamous NSCLC: KEYNOTE-021 cohort G update.** *Proc IASLC* 2017;**Abstract OA17.01**.

Langer CJ et al; KEYNOTE-021 Investigators. **Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: A randomised, phase 2 cohort of the open-label KEYNOTE-021 study.** *Lancet Oncol* 2016;17(11):1497-508.

Rittmeyer A et al; OAK Study Group. **Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): A phase 3, open-label, multicentre randomised controlled trial.** *Lancet* 2017;389(10066):255-65.

Matthew D Hellmann, MD

Antonia S et al. **Impact of tumor mutation burden on the efficacy of nivolumab or nivolumab + ipilimumab in small cell lung cancer: An exploratory analysis of CheckMate 032 (ID 11063).** *Proc IASLC*;**Abstract OA07.03a**.

Curran MA et al. **PD-1 and CTLA-4 combination blockade expands infiltrating T cells and reduces regulatory T and myeloid cells within B16 melanoma tumors.** *Proc Natl Acad Sci USA* 2010;107(9):4275-80.

Ford PM et al. **CheckMate 816: A phase 3, randomized, open-label trial of nivolumab plus ipilimumab vs platinum-doublet chemotherapy as neoadjuvant treatment for early-stage NSCLC.** *Proc ASCO* 2017;**Abstract TPS8577**.

Gangadhar TC et al. **Efficacy and safety of epacadostat plus pembrolizumab treatment of NSCLC: Preliminary phase I/II results of ECHO-202/KEYNOTE-037.** *Proc ASCO* 2017;**Abstract 9014**.

Hellmann MD et al. **Nivolumab plus ipilimumab as first-line treatment for advanced non-small-cell lung cancer (CheckMate 012): Results of an open-label, phase 1, multicohort study.** *Lancet Oncol* 2017;18(1):31-41.

Munn DH et al. **Prevention of allogeneic fetal rejection by tryptophan catabolism.** *Science* 1998;281(5380):1191-3.

Ott PA et al. **Pembrolizumab in patients with extensive-stage small-cell lung cancer: Results from the phase Ib KEYNOTE-028 study.** *J Clin Oncol* 2017;35(34):3823-9.