

# Leveraging the Immune System for Therapeutic Benefit in Non-Small Cell Lung Cancer: Scientific Insights, Clinical Applications and Future Directions

## Audio Program

### CME Information

#### TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, surgeons, radiation oncologists and other healthcare professionals involved in basic, translational and clinical cancer research or treatment.

#### OVERVIEW OF ACTIVITY

The past several years have seen an explosion in the emergence of new therapies that leverage the natural ability of the human body to attack and treat cancer. Known as cancer immunotherapies, these treatments are generating excitement all over the world as they have reshaped the management of lung cancer in previously unimagined ways. That being said, a number of controversies and questions remain with regard to the current application of these agents in clinical practice.

These proceedings from a satellite CME symposium held during the 2019 AACR Annual Meeting feature discussions with leading lung cancer investigators about the use of immunotherapy in the clinical care of patients with this disease. By providing information on important developments, this activity will assist medical oncologists and other healthcare professionals to address existing management uncertainties and determine the current and future roles of immune checkpoint inhibitors in lung cancer.

#### LEARNING OBJECTIVES

- Understand the biologic basis for the investigation of immune checkpoint inhibitors in combination with chemoradiation therapy for patients with nonmetastatic non-small cell lung cancer (NSCLC).
- Appreciate the recent FDA approval of anti-PD-L1 antibody consolidation therapy for patients with unresectable Stage III NSCLC who have not experienced disease progression after concurrent chemoradiation therapy, and discern how this strategy can be appropriately and safely integrated into routine clinical practice.
- Consider the available data and investigator perspectives regarding the efficacy of immune checkpoint inhibitors as single agents or in combination regimens for patients with metastatic NSCLC with or without targetable mutations.

- Recognize immune-related adverse events and other common side effects associated with the use of immune checkpoint inhibitors, and offer supportive strategies to minimize and manage these toxicities.
- Recall emerging data with novel approaches using immune checkpoint inhibitors for patients with NSCLC, and consider how these strategies may be applied in future clinical practice.

#### ACCREDITATION STATEMENT

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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:

### Corey J Langer, MD

Director of Thoracic Oncology  
Abramson Cancer Center  
Professor of Medicine  
Perelman School of Medicine  
University of Pennsylvania  
Philadelphia, Pennsylvania

**Advisory Committee and Consulting Agreements:** AbbVie Inc, Biodesix Inc, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Genentech, Lilly, Merck, Novartis, Pfizer Inc, Regeneron Pharmaceuticals Inc, Roche Laboratories Inc, Takeda Oncology; **Contracted Research:** Advantage Pharmaceuticals, GlaxoSmithKline, Inovio Pharmaceuticals Inc, Janssen Biotech Inc, Johnson & Johnson Pharmaceuticals, Lilly, Merck, Takeda Oncology; **Data and Safety Monitoring Board:** Amgen Inc, Incyte Corporation, Lilly, SWOG.

### Vali A Papadimitrakopoulou, MD

Jay and Lori Eisenberg Distinguished Professor  
Section Chief, Thoracic Medical Oncology  
Professor of Medicine  
Department of Thoracic/HN Medical Oncology  
The University of Texas MD Anderson Cancer Center  
Houston, Texas

**Advisory Committee:** AbbVie Inc, Araxes Pharma LLC, Arrys Therapeutics, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Clovis Oncology, Exelixis Inc, Gritstone Oncology, Guardant Health, Janssen Biotech Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Nektar, Novartis, Takeda Oncology, Tesaro, TRM Oncology; **Consulting Agreement:** Leads Biolabs Inc; **Contracted Research:** AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Checkmate Pharmaceuticals, Guardant Health, Incyte Corporation, Janssen Biotech

Inc, Lilly, Merck, Nektar, Novartis, Roche Laboratories Inc; **Speaker/Preceptorship:** Roche Laboratories Inc.

### Naiyer Rizvi, MD

Price Family Professor of Medicine at CUMC  
Columbia University Medical Center  
Director, Thoracic Oncology Program  
Co-Director, Immunotherapy in the Department of Medicine  
Research Director, Price Family Comprehensive Center for Chest Care at NewYork-Presbyterian Hospital  
New York, New York

**Consulting Agreements:** AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, EMD Serono Inc, Lilly, Merck, NeoGenomics, Novartis, Pfizer Inc, Regeneron Pharmaceuticals Inc, Roche Laboratories Inc; **Stock Ownership:** ARMO Biosciences, Bellicum Pharmaceuticals Inc, Gritstone Oncology.

### David R Spigel, MD

Chief Scientific Officer  
Program Director, Lung Cancer Research  
Sarah Cannon Research Institute  
Nashville, Tennessee

**Advisory Committee and Consulting Agreements:** AbbVie Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Evelo Biosciences, Foundation Medicine, Genentech, GlaxoSmithKline, Illumina, Lilly, Merck, Moderna Therapeutics, Nektar, Novartis, Pfizer Inc, PharmaMar, Precision Oncology LLC, Roche Laboratories Inc, Takeda Oncology, TRM Oncology; **Contracted Research:** AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Aeglea BioTherapeutics, Amgen Inc, ARMO Biosciences, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Celldex Therapeutics, Clovis Oncology, Daiichi Sankyo Inc, EMD Serono Inc, Foundation Medicine, G1 Therapeutics, Genentech, GlaxoSmithKline, GRAIL, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Nektar, Neon Therapeutics, Novartis, OncoGenex Pharmaceuticals Inc, Pfizer Inc, Roche Laboratories Inc, Takeda Oncology, Tesaro, Transgene, University of Texas Southwestern Medical Center Simmons Comprehensive Cancer Center.

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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

**Last review date:** June 2019

**Expiration date:** June 2020

## Select Publications

### Corey J Langer, MD

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

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

Butts C et al. **Tecemotide (L-BLP25) versus placebo after chemoradiotherapy for stage III non-small-cell lung cancer (START): A randomised, double-blind, phase 3 trial.** *Lancet Oncol* 2014;15(1):59-68.

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

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.

Lin S et al. **DETERRED: Phase II trial combining atezolizumab concurrently with chemoradiation therapy in locally advanced non-small cell lung cancer.** *J Thorac Oncol* 2018;13(10):S320-1.

Twyman-Saint Victor C et al. **Radiation and dual checkpoint blockade activate non-redundant immune mechanisms in cancer.** *Nature* 2015;520(7547):373-7.

Zeng J et al. **Anti-PD-1 blockade and stereotactic radiation produce long-term survival in mice with intracranial gliomas.** *Int J Radiat Oncol Biol Phys* 2013;86(2):343-9.

### Vali A Papadimitrakopoulou, MD

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

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

Boutros C et al. **Safety profiles of anti-CTLA-4 and anti-PD-1 antibodies alone and in combination.** *Nat Rev Oncol* 2016;13(8):473-86.

Brahmer JR et al. **Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology clinical practice guideline.** *J Clin Oncol* 2018;36(17):1714-68.

Cappelli LC et al. **Inflammatory arthritis and sicca syndrome induced by nivolumab and ipilimumab.** *Ann Rheum Dis* 2017;76(1):43-50.

De Bruyn P et al. **Immune checkpoint blockade for organ transplant patients with advanced cancer: How far can we go?** *Curr Opin Oncol* 2019;31(2):54-64.

El-Khoueiry AB et al. **Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): An open-label, non-comparative, phase 1/2 dose escalation and expansion trial.** *Lancet* 2017;389(10088):2492-502.

Leonardi GC et al. **Safety of programmed death-1 pathway inhibitors among patients with non-small-cell lung cancer and preexisting autoimmune disorders.** *J Clin Oncol* 2018;36(19):1905-12.

Naidoo J et al. **Inflammatory arthritis: A newly recognized adverse event of immune checkpoint blockade.** *Oncologist* 2017;22(6):627-30.

Naidoo J et al. **Pneumonitis in patients treated with anti-programmed death-1/programmed death ligand 1 therapy.** *J Clin Oncol* 2017;35(7):709-17.

Ryder M et al. **Endocrine-related adverse events following ipilimumab in patients with advanced melanoma: A comprehensive retrospective review from a single institution.** *Endocr Relat Cancer* 2014;21(2):371-81.

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

### David R Spigel, MD

Gandhi L et al. **Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer.** *N Engl J Med* 2018;378(22):2078-92.

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.

## Select Publications

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.

Paz-Ares L et al. **Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer.** *N Engl J Med* 2018;379(21):2040-51.

Reck M et al. **Pembrolizumab versus chemotherapy for pd-l1-positive non-small-cell lung cancer.** *N Engl J Med* 2016;375(19):1823-33.

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

### Naiyer Rizvi, MD

Abbosh C et al. **Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution.** *Nature* 2017;545(7655):446-51.

Diab A et al. **NKTR-214 (CD122-biased agonist) plus nivolumab in patients with advanced solid tumors: Preliminary phase 1/2 results of PIVOT.** *Proc ASCO* 2018;Abstract 3006.

Gandara DR et al. **Blood-based tumor mutational burden as a predictor of clinical benefit in non-small-cell lung cancer patients treated with atezolizumab.** *Nat Med* 2018;24(9):1441-8.

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.

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

Routy B et al. **Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors.** *Science* 2018;359(6371):91-7.

Strauss J et al. **Safety and activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF- $\beta$ , in patients with HPV associated cancers.** *Proc ASCO* 2018;Abstract 3007.

Whiteside TL et al. **Emerging opportunities and challenges in cancer immunotherapy.** *Clin Cancer Res* 2016;22(8):1845-55.