

Lung Cancer™

U P D A T E

Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

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Lung Cancer Update — A Continuing Medical Education Audio Series ---

OVERVIEW OF ACTIVITY

Traditional chemotherapy, surgery and radiation therapy have had a modest effect on long-term outcomes for patients with lung cancer. However, the advent of biologic and immunotherapeutic agents has led to recent improvements in disease-free and overall survival in select populations. In order to offer optimal patient care — including the option of clinical trial participation — clinicians must be well informed of these advances. Featuring information on the latest research developments, this program is designed to assist medical and radiation oncologists with the formulation of up-to-date strategies for the care of patients with lung cancer.

LEARNING OBJECTIVES

- Describe existing and emerging data on the efficacy and safety of immune checkpoint inhibitors in lung cancer, and consider this information when counseling patients regarding treatment options.
- Consider published safety and efficacy data with available and emerging therapeutic strategies, and appropriately incorporate targeted therapies into the care of patients with identified tumor driver mutations or alterations.
- Recognize the recent FDA approvals of nivolumab, pembrolizumab and ramucirumab for patients with metastatic non-small cell lung cancer (NSCLC), and discern how these agents can be safely administered to appropriate patients with squamous and nonsquamous disease.
- Describe mechanisms of tumor resistance to approved and investigational ALK inhibitors, and identify therapeutic opportunities to circumvent this process.

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SELECT PUBLICATIONS

A phase 2 study of MK-3475 in patients with metastatic melanoma and non-small cell lung cancer with untreated brain metastases. [NCT02085070](#)

A phase III, open-label, randomized study of MPDL3280A (anti-PD-L1 antibody) in combination with carboplatin + paclitaxel with or without bevacizumab compared with carboplatin + paclitaxel + bevacizumab in chemotherapy-naïve patients with stage IV non-squamous non-small cell lung cancer (NSCLC). [NCT02366143](#)

A trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum-doublet chemotherapy, compared to platinum doublet chemotherapy in patients with stage IV non-small cell lung cancer (NSCLC) (CheckMate 227). [NCT02477826](#)

An open-label, multicenter, phase 1 study of ramucirumab plus pembrolizumab in patients with locally advanced and unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma, non-small cell lung cancer, or transitional cell carcinoma of the urothelium. [NCT02443324](#)

An open-label, single arm phase II study of nivolumab in combination with ipilimumab as first line-therapy in stage IV non-small cell lung cancer (NSCLC). [NCT02659059](#)

Fehrenbacher L et al. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): A multicentre, open-label, phase 2 randomised controlled trial. *Lancet* 2016;387(10030):1837–46.

Gadgeel SM et al. Safety and activity of alectinib against systemic disease and brain metastases in patients with crizotinib-resistant ALK-rearranged non-small-cell lung cancer (AF-002JG): Results from the dose-finding portion of a phase 1/2 study. *Lancet Oncol* 2014;15(10):1119–28.

Garon EB et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): A multicentre, double-blind, randomised phase 3 trial. *Lancet* 2014;384(9944):665–73.

Hatcher JM et al. Discovery of inhibitors that overcome the G1202R anaplastic lymphoma kinase resistance mutation. *J Med Chem* 2015;58(23):9296–308.

Herbst RS et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): A randomised controlled trial. *Lancet* 2016;387(10027):1540–50.

Herbst RS et al. Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients. *Nature* 2014;515(7528):563–7.

Larkins E et al. US Food and Drug Administration approval summary: Ramucirumab for the treatment of metastatic non-small cell lung cancer following disease progression on or after platinum-based chemotherapy. *Oncologist* 2015;20(11):1320–5.

Park K et al. Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): A phase 2B, open-label, randomised controlled trial. *Lancet Oncol* 2016;17(5):577–89.

Planchard D et al. A phase III study of MEDI4736 (M), an anti-PD-L1 antibody, in monotherapy or in combination with tremelimumab (T), versus standard of care (SOC) in patients (pts) with advanced non-small cell lung cancer (NSCLC) who have received at least two prior systemic treatment regimens (ARCTIC). *Proc ASCO* 2015;Abstract TPS8104.

Planchard D et al. Interim results of a phase II study of the BRAF inhibitor (BRAFi) dabrafenib (D) in combination with the MEK inhibitor trametinib (T) in patients (pts) with BRAF V600E mutated (mut) metastatic non-small cell lung cancer (NSCLC). *Proc ASCO* 2015;Abstract 8006.

Rizvi NA et al. Safety and efficacy of first-line nivolumab and ipilimumab in non-small cell lung cancer. 16th World Conference on Lung Cancer;Abstract ORAL02.05.

Shaw AT et al. Resensitization to rizotinib by the lorlatinib ALK resistance mutation L1198F. *N Engl J Med* 2016;374(1):54–61.

Yang JC et al. Afatinib versus cisplatin-based chemotherapy for EGFR mutation-positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): Analysis of overall survival data from two randomised, phase 3 trials. *Lancet Oncol* 2015;16(2):141–51.

QUESTIONS (PLEASE CIRCLE ANSWER):

1. Adverse events associated with combination therapy with the anti-CTLA-4 antibody tremelimumab and the anti-PD-1 antibody durvalumab for patients with advanced NSCLC include _____.
 - a. Diarrhea
 - b. Pancreatitis
 - c. Both a and b
2. A Phase III trial evaluating docetaxel with or without ramucirumab for patients with Stage IV NSCLC after disease progression on a platinum-based regimen demonstrated a statistically significant improvement in survival with the addition of ramucirumab for patients with _____ disease.
 - a. Nonsquamous
 - b. Squamous
 - c. Both a and b
 - d. Neither a nor b
3. Analysis of overall survival in the Phase III LUX-Lung 3 and LUX-Lung 6 trials demonstrated a significant difference between afatinib and cisplatin-based chemotherapy as first-line therapy for patients with advanced adenocarcinoma of the lung harboring the _____ EGFR mutation.
 - a. Exon 19 deletion
 - b. L858R exon 21
 - c. Both a and b
4. The Phase II POPLAR trial evaluating atezolizumab versus docetaxel for previously treated advanced NSCLC reported a survival benefit with atezolizumab for patients with high levels of PD-L1 expression in their _____.
 - a. Tumor cells
 - b. Tumor-infiltrating immune cells
 - c. Both a and b
5. The anti-PD-1 antibodies nivolumab and pembrolizumab are both FDA approved for previously treated NSCLC, but the approved use of pembrolizumab requires that the patient's tumor express PD-L1.
 - a. True
 - b. False
6. Which of the following ALK inhibitors penetrates the central nervous system (CNS) well and thus exhibits significant activity in patients with NSCLC and CNS metastases?
 - a. Alectinib
 - b. Crizotinib
 - c. Both a and b
7. Lorlatinib (PF-06463922) is an investigational agent in the treatment of NSCLC and a potent inhibitor of _____.
 - a. PD-1
 - b. EGFR
 - c. ALK
8. The upper gastrointestinal tract side effects associated with ceritinib can be mitigated by dose reduction.
 - a. True
 - b. False
9. A Phase II trial presented by Planchard and colleagues at ASCO 2015 evaluating dabrafenib alone or in combination with trametinib for patients with BRAF V600E mutation-positive metastatic NSCLC demonstrated greater efficacy with the combination versus dabrafenib alone.
 - a. True
 - b. False
10. Patients with nonsquamous lung cancer should be tested routinely for which of the following tumor genetic alterations regardless of smoking history?
 - a. ALK
 - b. EGFR
 - c. ROS1
 - d. All of the above

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lung Cancer Update — Issue 2, 2016

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
POPLAR: Results of a Phase II trial evaluating atezolizumab versus docetaxel for patients with previously treated advanced NSCLC	4 3 2 1	4 3 2 1
Incorporation of immune checkpoint inhibitors into the treatment algorithm for patients with NSCLC	4 3 2 1	4 3 2 1
Mechanisms of resistance to ALK inhibitors and strategies to overcome resistance	4 3 2 1	4 3 2 1
Evaluation of anti-PD-1/PD-L1 antibodies (eg, pembrolizumab, atezolizumab) in combination with anti-VEGF agents (eg, bevacizumab, ramucirumab) for patients with advanced NSCLC	4 3 2 1	4 3 2 1
Interim results of a Phase II trial evaluating dabrafenib with trametinib for BRAF V600E mutation-positive metastatic NSCLC	4 3 2 1	4 3 2 1

Practice Setting:

- ☐ Academic center/medical school ☐ Community cancer center/hospital ☐ Group practice
☐ Solo practice ☐ Government (eg, VA) ☐ Other (please specify).....

Approximately how many new patients with lung cancer do you see per year? patients

Was the activity evidence based, fair, balanced and free from commercial bias?

- ☐ Yes ☐ No If no, please explain:

Please identify how you will change your practice as a result of completing this activity (select all that apply).

- ☐ This activity validated my current practice
☐ Create/revise protocols, policies and/or procedures
☐ Change the management and/or treatment of my patients
☐ Other (please explain):

If you intend to implement any changes in your practice, please provide 1 or more examples:

.....

The content of this activity matched my current (or potential) scope of practice.

- ☐ Yes ☐ No If no, please explain:

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Describe existing and emerging data on the efficacy and safety of immune checkpoint inhibitors in lung cancer, and consider this information when counseling patients regarding treatment options.....4 3 2 1 N/M N/A
- Consider published safety and efficacy data with available and emerging therapeutic strategies, and appropriately incorporate targeted therapies into the care of patients with identified tumor driver mutations or alterations.....4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

As a result of this activity, I will be able to:

- Recognize the recent FDA approvals of nivolumab, pembrolizumab and ramucirumab for patients with metastatic non-small cell lung cancer (NSCLC), and discern how these agents can be safely administered to appropriate patients with squamous and nonsquamous disease.4 3 2 1 N/M N/A
- Describe mechanisms of tumor resistance to approved and investigational ALK inhibitors, and identify therapeutic opportunities to circumvent this process.4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

.....

.....

PART 2 — Please tell us about the faculty and editor for this educational activity

	4 = Excellent	3 = Good	2 = Adequate	1 = Suboptimal	
Faculty	Knowledge of subject matter				Effectiveness as an educator
Roy S Herbst, MD, PhD	4	3	2	1	4 3 2 1
Alice Shaw, MD, PhD	4	3	2	1	4 3 2 1
Editor	Knowledge of subject matter				Effectiveness as an educator
Neil Love, MD	4	3	2	1	4 3 2 1

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