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Lung Cancer™ UPDATE

Conversations with Oncology Investigators

Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

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ABIM CME MOC ACCREDITED

CME Certified

Lung Cancer™ UPDATE

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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

- 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.
- Appraise emerging research data documenting the benefits and risks of sequential anti-PD-L1 antibody therapy for patients with locally advanced, unresectable NSCLC who have not experienced disease progression after standard platinum-based chemotherapy concurrent with radiation therapy.
- Develop a genomic testing algorithm to assist in identifying appropriate patients eligible for protocol and clinical targeted 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.
- Educate patients about the side effects associated with recently approved novel agents and immunotherapeutic approaches, and provide preventive strategies to reduce or ameliorate 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.

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Interview with Matthew D Hellmann, MD

Tracks 1-26

Interview with Lecia V Sequist, MD, MPH

Tracks 1-17

Track 1	**Case:** A 75-year-old woman and former smoker with recurrent squamous cell carcinoma (SCC) of the lung is found to harbor a MET exon 14 skipping mutation and receives crizotinib
Track 2	Perspective on the PACIFIC trial results
Track 3	Activity of gemcitabine monotherapy in SCC of the lung
Track 4	Incidence of MET exon 14 skipping mutations in SCC of the lung; response to crizotinib
Track 5	Acquired resistance to crizotinib in patients with NSCLC and MET exon 14 skipping mutations
Track 6	**Case:** A 50-year-old woman and never smoker with advanced adenocarcinoma of the lung and an EGFR L858R mutation
Track 7	Efficacy and tolerability of afatinib for metastatic EGFR L858R mutation-positive adenocarcinoma of the lung
Track 8	Activity of osimertinib in patients with leptomeningeal disease from EGFR-mutated advanced NSCLC
Track 9	FLAURA study results: Osimertinib versus erlotinib or gefitinib as first-line therapy for EGFR-mutated advanced NSCLC
Track 10	Clinical implications of the FLAURA trial results on T790M resistance mutation testing
Track 11	Efficacy of immune checkpoint inhibitors versus chemotherapy in patients with EGFR wild-type versus mutated NSCLC
Track 12	**Case:** A 68-year-old woman and moderate smoker with newly diagnosed metastatic adenocarcinoma of the lung, no targetable mutations and a high PD-L1 tumor proportion score (TPS)
Track 13	Pseudoprogression in patients receiving immune checkpoint inhibitors
Track 14	Re-treatment with immunotherapy after immune-related toxicity in patients who receive anti-PD-1 antibodies
Track 15	**Case:** A 57-year-old man and former smoker with symptomatic KRAS mutation-positive adenocarcinoma of the lung and a high PD-L1 TPS
Track 16	Perspective on the clinical utility of ramucirumab or bevacizumab in advanced NSCLC
Track 17	**Case:** A 63-year-old woman with heavily pretreated EGFR L858R mutation-positive adenocarcinoma of the lung who expresses interest in nivolumab/ipilimumab

Video Program

View the corresponding video interviews with (from left) Drs Hellmann and Sequist by Dr Love at www.ResearchToPractice.com/LCU118/Video

SELECT PUBLICATIONS

A phase I/II study of MK-3475 (SCH900475) in combination with chemotherapy or immunotherapy in patients with locally advanced or metastatic non-small cell lung carcinoma. NCT02039674

A phase III, open-label, randomized study of atezolizumab (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. NCT02366143

A phase III randomized, open-label, multi-center, global study of MEDI4736 in combination with tremelimumab therapy or MEDI4736 monotherapy versus standard of care platinum-based chemotherapy in first line treatment of patients with advanced or metastatic non small-cell lung cancer (NSCLC) (MYSTIC). NCT02453282

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

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

Chaft JE et al. **Neoadjuvant nivolumab in early-stage, resectable non-small cell lung cancers.** *Proc ASCO* 2017;**Abstract 8508**.

Goldman JW et al. **Nivolumab (N) plus ipilimumab (I) as first-line (1L) treatment for advanced (adv) NSCLC: 2-yr OS and long-term outcomes from CheckMate 012.** *Proc ASCO* 2017;**Abstract 9093**.

Heist RS et al. **Acquired resistance to crizotinib in NSCLC with MET exon 14 skipping.** *J Thorac Oncol* 2016;11(8):1242-5.

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**.

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.

Lee CK et al. **Checkpoint inhibitors in metastatic EGFR-mutated non-small cell lung cancer — A meta-analysis.** *J Thorac Oncol* 2017;12(2):403-7.

Leonardi GC et al. **Use of PD-1 pathway inhibitors among patients with non-small cell lung cancer (NSCLC) and preexisting autoimmune disorders.** *Proc ASCO* 2017;**Abstract 9081**.

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.

Osorio JC et al. **Antibody-mediated thyroid dysfunction during T-cell checkpoint blockade in patients with non-small-cell lung cancer.** *Ann Oncol* 2017;28(3):583-9.

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**.

Rai R et al. **Immunotherapy in patients with concurrent solid organ transplant, HIV, and hepatitis B and C.** *Proc ESMO* 2017;**Abstract 11489PD**.

Ramalingam SS et al. **Osimertinib vs standard of care (SoC) EGFR-TKI as first-line therapy in patients (pts) with EGFRm advanced NSCLC: FLAURA.** *Proc ESMO* 2017;**Abstract LBA2_PR**.

Sabari JK et al. **PD-L1 expression and response to immunotherapy in patients with *MET* exon 14-altered non-small cell lung cancers (NSCLC).** *Proc ASCO* 2017;**Abstract 8512**.

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**.

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.

Yang JCH et al. **Osimertinib activity in patients (pts) with leptomeningeal (LM) disease from non-small cell lung cancer (NSCLC): Updated results from BLOOM, a phase I study.** *Proc ASCO* 2016;**Abstract 9002**.

Zalcman G et al. **Second or 3rd line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Updated results of the IFCT-1501 MAPS2 randomized phase 2 trial.** *Proc ESMO* 2017;**Abstract LBA58_PR**.

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Which of the following immune-related toxicities is most common among patients with NSCLC treated with an anti-PD-1 antibody?**
   a. Colitis
   b. Pneumonitis
   c. Pruritus
   d. Thyroid dysfunction

2. **Patients with NSCLC who receive anti-PD-1/PD-L1 antibodies and experience treatment-associated pneumonitis can develop this complication at any time during treatment.**
   a. True
   b. False

3. **Results of the Phase III FLAURA study comparing first-line osimertinib to either erlotinib or gefitinib for patients with advanced EGFR-mutant NSCLC demonstrated a significant improvement in progression-free survival for patients who received osimertinib.**
   a. True
   b. False

4. **A study presented at ASCO 2017 evaluating neoadjuvant nivolumab for patients with early-stage, resectable NSCLC found that nivolumab _____ delay surgery.**
   a. Did
   b. Did not

5. **Which of the following categories reflects the mechanism of action of durvalumab?**
   a. Antibody-drug conjugate
   b. Anti-PD-1 antibody
   c. Anti-PD-L1 antibody

6. **Osimertinib _____ marked activity in patients with leptomeningeal metastases from EGFR mutation-positive advanced NSCLC.**
   a. Does not exhibit
   b. Exhibits

7. **The Phase III MYSTIC trial evaluating durvalumab and tremelimumab versus platinum-based chemotherapy for patients with previously untreated metastatic NSCLC _____ a statistically significant improvement in progression-free survival for patients who received the anti-PD-L1/CTLA-4 antibody combination.**
   a. Demonstrated
   b. Did not demonstrate

8. **A poster discussion presented by Hellmann and colleagues at the 2017 ASCO meeting demonstrated that among patients with NSCLC who developed immune-related adverse events (irAEs) but experienced disease improvement, re-treatment with immunotherapy was associated with recurrent or new irAEs in 50% of cases.**
   a. True
   b. False

9. **Results of the Phase III PACIFIC trial did not demonstrate a statistically significant improvement in progression-free survival with the addition of durvalumab compared to placebo after chemoradiation therapy for patients with Stage III NSCLC.**
   a. True
   b. False

10. **Although most of the major targetable mutations identified to date in lung cancer are predominantly found in patients with adenocarcinoma, _____ are more common in SCC of the lung as compared to the other driver mutations.**
    a. ALK rearrangements
    b. EGFR mutations
    c. MET exon 14 skipping mutations
    d. ROS1 rearrangements

EDUCATIONAL ASSESSMENT AND CREDIT FORM

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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
PACIFIC: Results of a Phase III trial of durvalumab as sequential treatment for locally advanced, unresectable NSCLC	4 3 2 1	4 3 2 1
Results of the Phase III FLAURA trial: Improvement in progression-free survival and tolerability with osimertinib versus erlotinib or gefitinib as first-line therapy for EGFR-mutated advanced NSCLC	4 3 2 1	4 3 2 1
Safety of re-treatment with immunotherapy after immune-related toxicity in patients with NSCLC treated with immune checkpoint inhibitors	4 3 2 1	4 3 2 1
Incidence of MET exon 14 skipping mutations in SCC of the lung	4 3 2 1	4 3 2 1
Correlation between high mutational burden, high PD-L1 TPS and enriched response rate to first-line nivolumab on the Phase III CheckMate 026 trial	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:

- 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..... 4 3 2 1 N/M N/A
- Appraise emerging research data documenting the benefits and risks of sequential anti-PD-L1 antibody therapy for patients with locally advanced, unresectable NSCLC who have not experienced disease progression after standard platinum-based chemotherapy concurrent with radiation therapy. ..... 4 3 2 1 N/M N/A
- Develop a genomic testing algorithm to assist in identifying appropriate patients eligible for protocol and clinical targeted treatment options..... 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:

- 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
- Educate patients about the side effects associated with recently approved novel agents and immunotherapeutic approaches, and provide preventive strategies to reduce or ameliorate these toxicities. . . . . 4 3 2 1 N/M N/A
- 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. . . . . 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:

. . . . . .

Would you recommend this activity to a colleague?

☐ Yes ☐ No

If no, please explain: . . . . . .

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**
Matthew D Hellmann, MD	4 3 2 1	4 3 2 1
Lecia V Sequist, MD, MPH	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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Lung Cancer™ UPDATE

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