

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™

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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

- Review research data documenting the efficacy and safety 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.
- Appreciate emerging research data documenting the benefits and risks of sequential anti-PD-L1 therapy for patients with unresectable Stage III NSCLC who have not experienced disease progression after chemoradiation therapy.
- 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.
- Formulate management strategies for small cell lung cancer, considering the contributory roles of local and systemic therapy in addition to current research evaluating novel immunotherapeutic and targeted approaches.
- Educate patients about the side effects of recently approved novel agents and immunotherapeutic approaches, and provide preventive strategies to reduce or ameliorate these toxicities.

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Interview with Suresh S Ramalingam, MD

Tracks 1-23

- Track 1** Mechanisms of resistance to osimertinib and management of non-small cell lung cancer (NSCLC) with EGFR tumor mutations in patients who experience disease progression on first-line osimertinib
- Track 2** Results of the Phase III IMpower150 trial: Atezolizumab and chemotherapy with or without bevacizumab versus bevacizumab and chemotherapy for chemotherapy-naïve metastatic nonsquamous NSCLC
- Track 3** Role of bevacizumab in combination with EGFR tyrosine kinase inhibitors (TKIs) for patients with NSCLC and EGFR tumor mutations
- Track 4** Emerging data with novel TKIs for patients with NSCLC and MET gene amplifications
- Track 5** Incidence and clinical significance of MET amplifications and MET exon 14 mutations
- Track 6** Use of liquid biopsies to detect mutations in patients with lung cancer
- Track 7** FLAURA study results: Osimertinib versus erlotinib or gefitinib as first-line therapy for advanced NSCLC with an EGFR tumor mutation
- Track 8** Ongoing evaluation of EGFR TKIs for Stage III NSCLC
- Track 9** Perspective on the use of osimertinib in the adjuvant setting
- Track 10** **Case:** A 62-year-old man and never smoker with Stage IV NSCLC and an EGFR exon 19 deletion receives osimertinib as first-line treatment
- Track 11** Response to osimertinib in patients with brain metastases
- Track 12** **Case:** A 44-year-old man and never smoker with metastatic NSCLC and an ALK rearrangement receives alectinib after disease progression on crizotinib with an anti-PD-1 antibody
- Track 13** ALTA-1L: A Phase III trial evaluating brigatinib versus crizotinib for advanced NSCLC with an ALK rearrangement
- Track 14** Efficacy and tolerability of lorlatinib in patients with NSCLC and an ALK rearrangement
- Track 15** **Case:** A 52-year-old woman and nonsmoker with metastatic NSCLC and a BRAF V600E tumor mutation receives dabrafenib and trametinib as second-line therapy
- Track 16** Use of targeted therapy as first-line treatment for patients with NSCLC
- Track 17** **Case:** A 58-year-old man with locally advanced squamous cell carcinoma of the lung receives durvalumab as consolidation therapy after chemoradiation therapy
- Track 18** Overall survival with the addition of durvalumab to chemoradiation therapy for patients with Stage III NSCLC
- Track 19** Pulmonary toxicity associated with durvalumab
- Track 20** Ongoing investigation of immune checkpoint inhibitors in the adjuvant setting
- Track 21** Management of metastatic small cell lung cancer
- Track 22** Novel agents under investigation for small cell lung cancer
- Track 23** Emerging research aimed at enhancing the efficacy of immune checkpoint inhibitors

Interview with Jamie E Chافت, MD

Tracks 1-26

- Track 1** **Case:** A 54-year-old woman and never smoker presenting with arthralgias, digital clubbing and leg edema is diagnosed with Stage IIIA NSCLC and an EGFR exon 19 deletion
- Track 2** Evaluation of anti-PD-1/PD-L1 antibodies as neoadjuvant therapy for NSCLC
- Track 3** Predictors of clinical benefit from neoadjuvant therapy with immune checkpoint inhibitors

Interview with Dr Chaff (continued)

- Track 4** Selection of patients for neoadjuvant therapy with anti-PD-1/PD-L1 antibodies
- Track 5** Choice of adjuvant therapy for patients with NSCLC and an EGFR tumor mutation
- Track 6** Risks and benefits with osimertinib in the adjuvant setting
- Track 7** Status of the Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST) for patients with early-stage lung cancer
- Track 8** Results of the Phase III SELECT trial of adjuvant erlotinib for resected NSCLC with an EGFR tumor mutation
- Track 9** **Case:** A 59-year-old man and former smoker with unresectable, Stage III NSCLC receives durvalumab as consolidation therapy after chemoradiation therapy
- Track 10** Management of superior vena cava syndrome in patients with lung cancer
- Track 11** Activity and tolerability of durvalumab as consolidation therapy
- Track 12** Perspective on the results of the PACIFIC trial of durvalumab after chemoradiation therapy for Stage III NSCLC
- Track 13** Recognition and management of pneumonitis associated with durvalumab/radiation therapy
- Track 14** Impact of baseline steroids on the efficacy of PD-1/PD-L1 blockade in patients with NSCLC
- Track 15** Effects of tumor mutations and PD-L1 expression on response to checkpoint inhibitors
- Track 16** **Case:** A 68-year-old woman and smoker experiences recurrent colitis after receiving nivolumab for metastatic NSCLC
- Track 17** Incidence and mitigation of diarrhea and colitis associated with checkpoint inhibitors
- Track 18** Management of metastatic nonsquamous NSCLC in the first-line setting
- Track 19** Perspective on the results of the Phase III IMpower150 study
- Track 20** Selection of first-line therapy for patients with metastatic squamous NSCLC
- Track 21** Risks and benefits of nivolumab with ipilimumab for metastatic NSCLC
- Track 22** Therapeutic approach for patients with metastatic small cell lung cancer
- Track 23** Duration of therapy with immune checkpoint inhibitors
- Track 24** Pseudoprogression and hyperprogression associated with immune checkpoint inhibitors
- Track 25** **Case:** A 64-year-old woman with metastatic NSCLC and an ALK rearrangement receives alectinib after developing intolerance to crizotinib
- Track 26** Efficacy and side effects of the ALK inhibitors alectinib, brigatinib and lorlatinib

Video Program

View the corresponding video interviews with (from left) Drs Ramalingam and Chaff by Dr Love at www.ResearchToPractice.com/LCU119/Video



SELECT PUBLICATIONS

- Ahn M et al. **TATTON phase Ib expansion cohort: Osimertinib plus savolitinib for patients with EGFR-mutant MET-amplified NSCLC after progression on prior EGFR-TKI.** *Proc WCLC* 2017;**Abstract OA 09.03.**
- Antonia SJ et al. **Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer.** *N Engl J Med* 2017;377(20):1919-29.
- Arbour KC et al. **Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer.** *J Clin Oncol* 2018;36(28):2872-8.
- Camidge DR et al. **Brigatinib versus crizotinib in ALK-positive non-small-cell lung cancer.** *N Engl J Med* 2018;379(21):2027-39.
- Camidge DR et al. **Updated efficacy and safety data from the global phase III ALEX study of alectinib (ALC) vs crizotinib (CZ) in untreated advanced ALK+ NSCLC.** *Proc ASCO* 2018;**Abstract 9043.**
- Chung HC et al. **Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158.** *Proc ASCO* 2018;**Abstract 8506.**
- Dudnik E et al. **BRAF mutant lung cancer: Programmed death ligand 1 expression, tumor mutational burden, microsatellite instability status, and response to immune check-point inhibitors.** *J Thorac Oncol* 2018;13(8):1128-37.
- Forde P et al. **Neoadjuvant PD-1 blockade in resectable lung cancer.** *N Engl J Med* 2018;378(21):1976-86.
- 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 in lung cancer with a high tumor mutational burden.** *N Engl J Med* 2018;378(22):2093-104.
- Kamphorst AO et al. **Rescue of exhausted CD8 T cells by PD-1-targeted therapies is CD28-dependent.** *Science* 2017;355(6332):1423-7.
- Lin JJ et al. **Brigatinib in patients with alectinib-refractory ALK-positive non-small cell lung cancer: A retrospective study.** *J Thorac Oncol* 2018;13(10):1530-8.
- Lopes G et al. **Pembrolizumab (pembro) versus platinum-based chemotherapy (chemo) as first-line therapy for advanced/metastatic NSCLC with a PD-L1 tumor proportion score (TPS) \geq 1%: Open-label, phase 3 KEYNOTE-042 study.** *Proc ASCO* 2018;**Abstract LBA4.**
- Magnuson WJ et al. **Management of brain metastases in tyrosine kinase inhibitor-naïve epidermal growth factor receptor-mutant non-small-cell lung cancer: A retrospective multi-institutional analysis.** *J Clin Oncol* 2017;35(10):1070-7.
- Paz-Ares LG et al. **Phase 3 study of carboplatin-paclitaxel/nab-paclitaxel (Chemo) with or without pembrolizumab (Pembro) for patients (Pts) with metastatic squamous (Sq) non-small cell lung cancer (NSCLC).** *Proc ASCO* 2018;**Abstract 105.**
- Pennell NA et al. **SELECT: A phase II trial of adjuvant erlotinib in patients with resected epidermal growth factor receptor-mutant non-small-cell lung cancer.** *J Clin Oncol* 2019;37(2):97-104.
- Ramalingam SS et al. **Mechanisms of acquired resistance to first-line osimertinib: Preliminary data from the phase III FLAURA study.** *Proc ESMO* 2018;**Abstract LBA50.**
- Ramalingam SS et al. **Osimertinib as first-line treatment of EGFR mutation-positive advanced non-small-cell lung cancer.** *J Clin Oncol* 2018;36(9):841-9.
- Rizvi H et al. **Molecular determinants of response to anti-programmed cell death (PD)-1 and anti-programmed death-ligand 1 (PD-L1) blockade in patients with non-small-cell lung cancer profiled with targeted next-generation sequencing.** *J Clin Oncol* 2018;36(7):633-41.
- Rusch VW et al. **Neoadjuvant atezolizumab in resectable non-small cell lung cancer (NSCLC): Initial results from a multicenter study (LCMC3).** *Proc ASCO* 2018;**Abstract 8541.**
- Shaw AT et al. **Efficacy of lorlatinib in patients (pts) with advanced ALK-positive non-small cell lung cancer (NSCLC) and ALK kinase domain mutations.** *Proc AACR* 2018;**Abstract CT044.**
- Socinski MA et al. **Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC.** *N Engl J Med* 2018;378(24):2288-301.
- Soria JC et al. **Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer.** *N Engl J Med* 2018;378(2):113-25.

QUESTIONS (PLEASE CIRCLE ANSWER):

- A recent paper in the *Journal of Clinical Oncology* comparing the CNS activity of osimertinib to that of standard EGFR TKIs (gefitinib or erlotinib) in patients with NSCLC and EGFR tumor mutations demonstrated _____ in the osimertinib arm.
 - Higher response rates
 - Lower risk of disease progression in the CNS
 - Both a and b
- Results of the Phase III FLAURA study comparing first-line osimertinib to either erlotinib or gefitinib for patients with advanced NSCLC and EGFR tumor mutations demonstrated a significant improvement in progression-free survival (PFS) with osimertinib.
 - True
 - False
- The TATTON trial is investigating the combination of the EGFR inhibitor osimertinib with the MET inhibitor _____ for patients with advanced NSCLC, EGFR tumor mutations and MET amplification.
 - Dacomitinib
 - Savolitinib
 - Erlotinib
- Which of the following categories reflects the mechanism of action of rovalpituzumab tesirine?
 - Antibody-drug conjugate
 - Anti-PD-1 antibody
 - Anti-PD-L1 antibody
 - RET inhibitor
- Osimertinib _____ marked activity in patients with leptomeningeal metastases from advanced NSCLC with EGFR tumor mutations.
 - Does not exhibit
 - Exhibits
- In the Phase III IMpower150 trial, the combination of atezolizumab/chemotherapy/bevacizumab did not demonstrate a significant improvement in PFS for the subset of patients with EGFR and ALK alterations.
 - True
 - False
- In the ALTA-1L trial evaluating _____ versus crizotinib for patients with NSCLC and ALK rearrangements, the reduction in the risk of disease progression or death in the experimental arm was approximately 50%.
 - Alectinib
 - Brigatinib
 - Lorlatinib
- The Phase III PACIFIC trial of durvalumab for patients with locally advanced, unresectable NSCLC without disease progression after definitive platinum-based chemoradiation therapy demonstrated a statistically significant improvement in _____ with durvalumab compared to placebo.
 - Overall survival
 - PFS
 - Both a and b
 - Neither a nor b
- Which of the following categories reflects the mechanism of action of the recently FDA-approved agent lorlatinib?
 - ALK inhibitor
 - Antibody-drug conjugate
 - Anti-PD-1/PD-L1 antibody
 - MET inhibitor
 - RET inhibitor
- Mutations in the MET exon 14 gene _____.
 - Occur in approximately 3% to 4% of patients with nonsquamous NSCLC
 - Are not sensitive to crizotinib
 - Both a and b

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lung Cancer Update — Volume 15, Issue 3

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
Results of the Phase III FLAURA trial comparing osimertinib to erlotinib or gefitinib as first-line therapy for advanced NSCLC with an EGFR tumor mutation; nonresearch role of osimertinib	4 3 2 1	4 3 2 1
Key efficacy and safety findings from the ALTA-1L trial evaluating brigatinib versus crizotinib for advanced NSCLC with an ALK rearrangement	4 3 2 1	4 3 2 1
Activity and tolerability of durvalumab as sequential treatment for locally advanced, unresectable Stage III NSCLC	4 3 2 1	4 3 2 1
Use of liquid biopsies to detect mutations in patients with lung cancer	4 3 2 1	4 3 2 1
Benefit of the atezolizumab/chemotherapy/bevacizumab combination for patients with EGFR and ALK mutations in the Phase III IMpower150 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:

- Review research data documenting the efficacy and safety 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
- Appreciate emerging research data documenting the benefits and risks of sequential anti-PD-L1 therapy for patients with unresectable Stage III NSCLC who have not experienced disease progression after chemoradiation therapy. 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:

- Formulate management strategies for small cell lung cancer, considering the contributory roles of local and systemic therapy in addition to current research evaluating novel immunotherapeutic and targeted approaches..... 4 3 2 1 N/M N/A
- Educate patients about the side effects of 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

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			
Suresh S Ramalingam, MD	4	3	2	1	4	3	2	1
Jamie E Chافت, MD	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™

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