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

FACULTY INTERVIEWS
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Justin F Gainor, MD

EDITOR
Neil Love, MD
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 lung cancer to determine the current and/or potential utility of each in clinical practice.
• Formulate management strategies for small cell lung cancer, considering systemic therapy in addition to current research studies evaluating novel immunotherapeutic and targeted approaches.
• Appreciate the FDA approval of durvalumab and available Phase III data documenting the benefit of sequential anti-PD-L1 therapy after the completion of chemoradiation therapy for unresectable Stage III non-small cell lung cancer, and consider the role of this therapeutic approach for appropriate patients.
• 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.

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**FACULTY**  —  Dr Spigel has no relevant conflicts of interest to disclose. The following faculty (and his spouse/partner) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: Dr Gainor — Consulting Agreements: Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc/Takeda Oncology, Array BioPharma Inc, Bristol-Myers Squibb Company, Genentech, Pfizer Inc, Theravance Biopharma; Honoraria: Genentech, Incyte Corporation, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc.


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Interview with David R Spigel, MD

Tracks 1-20

Track 1  **Case:** A 73-year-old man with recurrent small cell lung cancer (SCLC) receives ipilimumab/nivolumab on a clinical trial
Track 2  Management of immune checkpoint inhibitor-associated rash
Track 3  Correlation between toxicity and treatment benefit for patients receiving immune checkpoint inhibitors
Track 4  Clinical experience with dermatologic side effects of checkpoint inhibitors
Track 5  Second-line therapy options for metastatic SCLC
Track 6  Perspective on ipilimumab/nivolumab dosing and therapy-associated toxicities
Track 7  Activity, side effects and ongoing investigation of the antibody-drug conjugate rovalpituzumab tesirine (Rova-T) in DLL3-positive SCLC
Track 8  Clinical experience with Rova-T-associated edema
Track 9  Results of the Phase III KEYNOTE-407 trial evaluating the addition of pembrolizumab to carboplatin with paclitaxel or nab paclitaxel as first-line therapy for metastatic squamous non-small cell lung cancer (NSCLC)
Track 10  **KEYNOTE-042:** Overall survival benefit with pembrolizumab versus platinum-based chemotherapy as first-line treatment for locally advanced or metastatic NSCLC with a PD-L1 tumor proportion score (TPS) of 1% or higher
Track 11  Clinical implications of the KEYNOTE-042 results; perspective on the future clinical utility of TPS
Track 12  Evolution of first-line checkpoint inhibitor-based treatment for metastatic nonsquamous NSCLC with and without targetable tumor mutations
Track 13  Selection of checkpoint inhibitor-based regimens for patients experiencing disease progression on an EGFR tyrosine kinase inhibitor (TKI)
Track 14  **Case:** A 57-year-old man with Stage IIIA squamous NSCLC receives chemoradiation therapy followed by durvalumab
Track 15  Ongoing studies of checkpoint inhibitors in the (neo)adjuvant setting
Track 16  PACIFIC trial: Efficacy and tolerability of durvalumab after chemoradiation therapy for unresectable Stage III NSCLC
Track 17  Management of chemoradiation therapy-associated pneumonitis
Track 18  Perspective on the synergy of durvalumab and chemoradiation therapy
Track 19  Use of chemoradiation therapy followed by durvalumab for patients with Stage III NSCLC and a targetable tumor mutation
Track 20  **Case:** A woman in her early fifties with advanced “pan-negative” nonsquamous NSCLC experiences a near complete response with 1 dose of ipilimumab/nivolumab

Interview with Justin F Gainor, MD

Tracks 1-17

Track 1  **Case:** A 76-year-old man and never smoker presents with metastatic NSCLC with an EGFR L858R tumor mutation, a low PD-L1 TPS and brain metastases and receives first-line osimertinib
Track 2  Activity and tolerability of first-line osimertinib
Track 3  Stereotactic radiosurgery, whole-brain radiation therapy (WBRT) and EGFR TKIs for patients with EGFR tumor mutations and brain metastases
Track 4  Incidence and pathophysiology of neurocognitive effects of WBRT
Track 5  Optimal sequencing of EGFR TKIs
Interview with Dr Gainor (continued)

Track 6  Mechanism of action, benefits and limitations of the second-generation EGFR inhibitor dacomitinib

Track 7  Investigational strategies for patients experiencing disease progression on osimertinib

Track 8  Bevacizumab with erlotinib as first-line therapy for patients with metastatic NSCLC and an EGFR tumor mutation

Track 9  Rationale for combining first- and third-generation EGFR TKIs to potentially treat tumors with resistance mutations

Track 10 Case: A 57-year-old woman and never smoker with crizotinib-refractory NSCLC with an ALK rearrangement receives alectinib

Track 11  Sequencing of ALK inhibitors for patients with metastatic NSCLC with an ALK rearrangement

Track 12  Second-line therapy options for patients with metastatic NSCLC with an ALK rearrangement

Track 13 Case: A 64-year-old woman and never smoker with NSCLC with brain and bone metastases initially treated with carboplatin/pemetrexed is found to harbor a RET rearrangement

Track 14 Case: A 48-year-old man with heavily pretreated nonsquamous NSCLC whose tumor is positive for an NTRK gene fusion receives entrectinib on a clinical trial

Track 15  Efficacy of the TRK inhibitors entrectinib and larotrectinib

Track 16 Case: A 71-year-old man and 35 pack-year smoker with metastatic nonsquamous NSCLC and a BRAF V600E tumor mutation, renal insufficiency and a high TPS receives dabrafenib/trametinib

Track 17  Consideration of immune checkpoint inhibitor-based regimens as second-line therapy for patients with metastatic disease and renal insufficiency

Video Program

View the corresponding video interviews with (from left) Drs Spigel and Gainor by Dr Love at www.ResearchToPractice.com/LCU318/Video

Have Questions or Cases You Would Like Us to Pose to the Faculty?

Submit them to us via Facebook or Twitter and we will do our best to get them answered for you Facebook.com/ResearchToPractice or Twitter @DrNeilLove
SELECT PUBLICATIONS

A study of carboplatin plus etoposide with or without atezolizumab in participants with untreated extensive-stage (ES) small cell lung cancer (SCLC) (IMpower133). NCT02763579
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.
Jiyeong Lin J et al. Long-term efficacy and outcomes with sequential crizotinib followed by alectinib in ALK+ NSCLC. Proc ASCO 2018;Abstract 9093.
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.
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.
1. The Phase III FLAURA study comparing first-line osimertinib to either erlotinib or gefitinib for advanced NSCLC with an EGFR tumor mutation demonstrated a significant improvement in progression-free survival (PFS) for patients who received osimertinib.
   a. True
   b. False

2. Which of the following categories reflects the mechanism of action of Rova-T?
   a. Antibody-drug conjugate
   b. Anti-PD-1 antibody
   c. RET inhibitor

3. Results of a Phase III trial evaluating dacomitinib versus gefitinib as first-line therapy for patients with locally advanced or metastatic NSCLC and an EGFR tumor mutation demonstrated a significant improvement in __________ with dacomitinib.
   a. Overall survival
   b. PFS
   c. Both a and b

4. The results of the Phase III IMpower150 trial of atezolizumab and/or bevacizumab added to carboplatin and paclitaxel as first-line therapy for patients with metastatic nonsquamous NSCLC failed to demonstrate any statistically significant improvement in overall survival or PFS with the addition of atezolizumab and bevacizumab to carboplatin/paclitaxel.
   a. True
   b. False

5. Results of the Phase III KEYNOTE-042 trial demonstrated a significant improvement in overall survival with single-agent pembrolizumab as first-line treatment for locally advanced or metastatic NSCLC in patients with a PD-L1 TPS of __________.
   a. 1% or higher
   b. 20% or higher
   c. 50% or higher
   d. All of the above

6. __________ is a second-generation ALK inhibitor that is currently FDA approved for the treatment of metastatic NSCLC with an ALK rearrangement.
   a. Alectinib
   b. Brigatinib
   c. Ceritinib
   d. All of the above

7. __________ is a promising investigational agent that targets TRK kinases in adult and pediatric patients with cancers harboring an NTRK gene fusion.
   a. Entrectinib
   b. Larotrectinib
   c. Both a and b

8. The Phase III KEYNOTE-407 trial evaluating the addition of pembrolizumab to carboplatin with paclitaxel or nab-paclitaxel as first-line therapy for metastatic squamous NSCLC demonstrated prolonged median overall survival and PFS with the addition of pembrolizumab to conventional chemotherapy across all PD-L1 expression subgroups.
   a. True
   b. False

9. The Phase III PACIFIC trial of durvalumab versus placebo for patients with locally advanced, unresectable NSCLC without disease progression after definitive platinum-based chemoradiation therapy demonstrated a statistically significant improvement in __________ with durvalumab.
   a. Overall survival
   b. PFS
   c. Objective response rate
   d. All of the above

10. Results of the global Phase III ALEX study evaluating alecinitib versus crizotinib demonstrated a significant PFS improvement with alecinitib for patients with __________ advanced NSCLC with an ALK rearrangement.
    a. Treatment-naive
    b. Previously treated
EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lung Cancer Update — Volume 15, Issue 2

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?

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<thead>
<tr>
<th>Topic</th>
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<th>AFTER</th>
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<tr>
<td>Results of the Phase III FLAURA trial and use of osimertinib as first-line therapy for advanced NSCLC with an EGFR tumor mutation</td>
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<td>Clinical implications of the KEYNOTE-042 trial results: Overall survival benefit with pembrolizumab versus platinum-based chemotherapy as first-line treatment for metastatic NSCLC with a PD-L1 TPS of 1% or higher</td>
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<td>Sequencing of FDA-approved ALK inhibitors for NSCLC with an ALK rearrangement</td>
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<td>PACIFIC: Results of a Phase III trial of durvalumab as sequential treatment for locally advanced, unresectable Stage III NSCLC</td>
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<td>Clinical implications of the Phase III KEYNOTE-407 trial evaluating the addition of pembrolizumab to carboplatin with paclitaxel or nab paclitaxel as first-line therapy for metastatic squamous NSCLC</td>
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Practice Setting:
- [ ] Academic center/medical school
- [ ] Community cancer center/hospital
- [ ] Group practice
- [ ] Solo practice
- [ ] Government (e.g., 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
  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
  Please explain: ........................................................................

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

<table>
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<th>4 = Yes</th>
<th>3 = Will consider</th>
<th>2 = No</th>
<th>1 = Already doing</th>
<th>N/M = LO not met</th>
<th>N/A = Not applicable</th>
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<td>As a result of this activity, I will be able to:</td>
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<td>• 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 lung cancer to determine the current and/or potential utility of each in clinical practice.</td>
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<td>• Formulate management strategies for small cell lung cancer, considering systemic therapy in addition to current research studies evaluating novel immunotherapeutic and targeted approaches.</td>
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<td>• Appreciate the FDA approval of durvalumab and available Phase III data documenting the benefit of sequential anti-PD-L1 therapy after the completion of chemoradiation therapy for unresectable Stage III non-small cell lung cancer, and consider the role of this therapeutic approach for appropriate patients.</td>
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EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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

- 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
- 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

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

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tr>
<td>David R Spigel, MD</td>
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<td>Justin F Gainor, MD</td>
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<th>Editor</th>
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<td>Neil Love, MD</td>
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REQUEST FOR CREDIT — Please print clearly

Name: ............................................................. Specialty: .............................................................

Professional Designation:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other: ..................................................

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I certify my actual time spent to complete this educational activity to be _________ hour(s).

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