Lingering Controversies and Emerging Therapeutic Strategies for Patients with Locally Advanced Non-Small Cell Lung Cancer

An Audio Review Journal for Radiation Oncologists

FACULTY INTERVIEWS

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This activity provides Category 1 CME that may be used as self-assessment credit toward Part 2 of the American Board of Radiology MOC Program.

CME Certified

Lung Cancer™ UPDATE

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OVERVIEW OF ACTIVITY

Non-small cell lung cancer (NSCLC) accounts for 84% of all lung cancer cases, and approximately one third of the patients in this population present with locally advanced, or Stage III, disease. Expected 5-year survival rates for these patients range from 36% (Stage IIIA) to 13% (Stage IIIC). Therefore, the clinical care of these individuals remains one of the most significant challenges in solid tumor oncology. Recent breakthroughs have led to the advent of new treatment modalities, and in order to offer optimal patient care, including the option of clinical trial participation, clinicians must be well informed of these advances.

Because of the heightened role of radiation oncologists in the multidisciplinary management of locally advanced NSCLC and the significant research developments currently unfolding, this CME program focuses specifically on meeting the educational needs of those specialists. By providing access to the latest data sets and expert perspectives, this activity will assist radiation oncologists in the formulation of up-to-date clinical management strategies for locally advanced NSCLC.

LEARNING OBJECTIVES

- Evaluate the benefits, risks and long-term outcomes associated with local and systemic treatment modalities for locally advanced NSCLC, and consider this information when counseling patients regarding current therapeutic recommendations.
- Consider available and emerging clinical data in the selection of the optimal technique and dose of radiation therapy for patients with locally advanced NSCLC.
- Understand the biologic basis for the investigation of immune checkpoint inhibitors in combination with chemoradiation therapy for patients with nonmetastatic 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.
- Recognize immune-related adverse events and other common side effects associated with the use of immune checkpoint inhibitors as consolidation therapy for patients with Stage III NSCLC, and offer supportive strategies to minimize and/or manage these toxicities.
- Recall the design of ongoing clinical trials evaluating novel therapeutic approaches for locally advanced NSCLC, and counsel appropriate patients about availability and participation.

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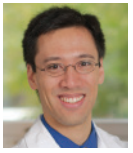

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Rimner** — Consulting Agreements: AstraZeneca Pharmaceuticals LP, Merck, Varian Medical Systems Inc; Contracted Research: AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Pfizer Inc, Varian Medical Systems Inc. **Dr Langer** — 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.

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Interview with Andreas Rimner, MD

Tracks 1-21

Track 1 Evaluation, staging and typical disease management approaches for patients with locally advanced non-small cell lung cancer (NSCLC)

Track 2 Selection and dose of postoperative radiation therapy (RT)

Track 3 Stereotactic body RT (SBRT) versus surgery for patients with early-stage NSCLC

Track 4 **Case:** A man in his mid-70s, a former smoker, with Stage IIIC adenocarcinoma of the lung receives durvalumab consolidation after chemoradiation therapy (CRT)

Track 5 Optimal design of the radiation treatment field; mitigation of RT-associated side effects

Track 6 Results of the Phase III RTOG-0617 trial evaluating carboplatin/paclitaxel in combination with standard- versus high-dose conformal RT, with or without cetuximab, for Stage III NSCLC

Track 7 Role of RT in enhancing tumor immunogenicity

Track 8 Avoiding safety concerns with the combination of CRT and immune checkpoint inhibitors

Track 9 Activity and tolerability of pembrolizumab after RT in patients with NSCLC on the Phase I KEYNOTE-001 trial

Track 10 PACIFIC trial: Efficacy and tolerability of durvalumab after CRT for patients with unresectable Stage III NSCLC

Track 11 Activity of durvalumab after CRT; diagnosis and management of pneumonitis associated with durvalumab/CRT

Track 12 Ongoing Phase II trial evaluating the activity and safety of nintedanib with prednisone for the treatment of radiation pneumonitis

Track 13 Incidence of pneumonitis with CRT alone and with the addition of durvalumab

Track 14 Survival outcomes and duration of consolidation therapy with durvalumab

Track 15 Ongoing evaluation of immune checkpoint inhibitors with concurrent RT with or without chemotherapy

Track 16 Activity of immune checkpoint inhibitors in the neoadjuvant setting

Track 17 Selection of the optimal dose and technique of RT for locally advanced NSCLC

Track 18 **Case:** A woman in her early 70s with unresectable Stage IIIB adenocarcinoma of the lung and a KRAS mutation receives CRT followed by durvalumab

Track 19 Clinical experience with the use of durvalumab after CRT

Track 20 **Case:** A woman in her mid-50s with Stage III adenocarcinoma of the lung and an EGFR mutation receives adjuvant osimertinib

Track 21 Increased RT precision with the merging of MRI and a linear accelerator

Interview with Corey J Langer, MD

Tracks 1-22

Track 1 **Case:** A woman in her mid-60s, a never smoker, with locally advanced, unresectable adenocarcinoma of the lung and an EGFR exon 18 tumor mutation receives CRT followed by consolidation durvalumab

Track 2 Clinical significance and prognostic relevance of microsatellite instability testing in the management of lung cancer

Track 3 Risk of recurrence after concurrent CRT for patients with Stage III NSCLC

Track 4 Improvement in progression-free and overall survival with the addition of consolidation durvalumab after CRT for patients with Stage III NSCLC on the PACIFIC trial

Track 5 Role of immune checkpoint inhibition in the treatment of locally advanced NSCLC with an EGFR tumor mutation

Track 6 Perspective on the use of EGFR tyrosine kinase inhibitors in the adjuvant or neoadjuvant setting for patients with locally advanced NSCLC and EGFR tumor mutations

Interview with Dr Langer (continued)

Track 7 Initial diagnostic workup and disease management for patients with locally advanced NSCLC

Track 8 RTOG-1308: An ongoing Phase III trial of photon versus proton CRT for patients with inoperable Stage II to Stage IIIB NSCLC

Track 9 Role of proton beam RT in the treatment of locally advanced NSCLC

Track 10 Rationale for the combination of RT and immune checkpoint inhibitors

Track 11 Risk of pneumonitis with CRT

Track 12 Design and results of the Phase III PACIFIC trial of durvalumab after CRT for unresectable Stage III NSCLC

Track 13 Monitoring and management of the toxicities associated with immune checkpoint inhibitors

Track 14 Use of durvalumab for patients with preexisting autoimmune disease and for transplant recipients

Track 15 Results from the Phase II Hoosier Cancer Research Network LUN14-179 trial of consolidation pembrolizumab after CRT for unresectable Stage III NSCLC

Track 16 Ongoing investigation of anti-PD-1/PD-L1 immune checkpoint inhibitors for locally advanced disease

Track 17 **Case:** A man in his mid-80s, a former heavy smoker with multiple comorbidities, is diagnosed with locally advanced squamous cell carcinoma of the lung with a high PD-L1 TPS (tumor proportion score)

Track 18 Use of liquid biopsies to detect targetable tumor mutations in patients with lung cancer

Track 19 **Case:** A man in his mid-50s, a former smoker, is diagnosed with Stage IIIA mixed adenosquamous carcinoma of the lung with TTF-1 and p40 tumor mutations

Track 20 Perspective on the use of anti-PD-1/PD-L1 antibodies as neoadjuvant therapy for patients with NSCLC

Track 21 **Case:** A man in his early 70s, a current smoker, with adenosquamous carcinoma of the lung and a KRAS mutation receives SBRT

Track 22 Optimal approach to RT for patients with locally advanced NSCLC

Video Program

View the corresponding video interviews with (from left) Drs Rimner and Langer by Dr Love at www.ResearchToPractice.com/LCURadOnc119/Video

SELECT PUBLICATIONS

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POST-TEST

Lingering Controversies and Emerging Therapeutic Strategies for Patients with Locally Advanced Non-Small Cell Lung Cancer

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The Phase III PACIFIC trial evaluating durvalumab versus placebo after CRT for patients with unresectable Stage III NSCLC demonstrated a significant improvement in _____ on the durvalumab arm.**
   a. Progression-free survival
   b. Overall survival
   c. Both a and b

2. **Which overall survival result was reported from the Phase III RTOG-0617 study evaluating standard-dose versus high-dose conformal RT with concurrent and consolidation chemotherapy with or without cetuximab for patients with newly diagnosed, inoperable Stage III NSCLC?**
   a. A benefit with the higher 74 Gray radiation dose
   b. No benefit with the addition of cetuximab
   c. Both a and b
   d. Neither a nor b

3. **Administration of durvalumab compared to placebo after CRT _____ result in a significantly higher rate of pneumonitis for patients with unresectable Stage III NSCLC on the Phase III PACIFIC trial.**
   a. Did
   b. Did not

4. **The rationale for the use of immune checkpoint inhibition after CRT for the treatment of lung cancer includes radiation-induced _____.**
   a. Release of tumor antigens
   b. Upregulation of PD-L1 on tumor cells
   c. Release of cytokines
   d. All of the above

5. **SBRT may be considered as an alternative treatment approach for patients with inoperable early-stage NSCLC and those for whom surgery would add considerable risk.**
   a. True
   b. False

6. **The single-arm Phase II LUN14-179 trial investigated consolidation therapy with the anti-PD-1 antibody _____ after CRT for patients with unresectable Stage III NSCLC.**
   a. Nivolumab
   b. Atezolizumab
   c. Pembrolizumab

7. **Which category best reflects the mechanism of action of nintedanib, currently being investigated for the treatment of radiation-induced pneumonitis?**
   a. Tyrosine kinase inhibitor
   b. Immune checkpoint inhibitor
   c. Anti-EGFR antibody

8. **A major advantage of proton therapy over traditional radiation techniques is the ability to precisely target tumors and limit the damage to surrounding healthy tissue.**
   a. True
   b. False

9. **What was the maximum duration of durvalumab therapy after CRT in the Phase III PACIFIC trial for patients with unresectable Stage III NSCLC?**
   a. Six months
   b. Nine months
   c. Twelve months

10. **A secondary analysis of the Phase I KEYNOTE-001 trial for patients with advanced NSCLC demonstrated longer progression-free survival with pembrolizumab for patients who had previously received RT in comparison to those who had not.**
    a. True
    b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lingering Controversies and Emerging Therapeutic Strategies for Patients with Locally Advanced Non-Small Cell Lung Cancer

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 trial: Efficacy of durvalumab after CRT for unresectable Stage III NSCLC	4 3 2 1	4 3 2 1
Side effects associated with the use of durvalumab as consolidation therapy after CRT for Stage III NSCLC	4 3 2 1	4 3 2 1
Key efficacy results from the Phase III RTOG-0617 study evaluating carboplatin/paclitaxel in combination with standard- versus high-dose conformal RT, with or without cetuximab, for Stage III NSCLC	4 3 2 1	4 3 2 1
Outcomes and ongoing evaluation of SBRT versus surgery for patients with early-stage NSCLC	4 3 2 1	4 3 2 1
Activity and tolerability of pembrolizumab consolidation after chemoradiation therapy for patients with unresectable Stage III NSCLC in the Phase II Hoosier Cancer Research Network LUN 14-179 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:

- Evaluate the benefits, risks and long-term outcomes associated with local and systemic treatment modalities for locally advanced NSCLC, and consider this information when counseling patients regarding current therapeutic recommendations. . . . . 4 3 2 1 N/M N/A
- Consider available and emerging clinical data in the selection of the optimal technique and dose of radiation therapy for patients with locally advanced NSCLC. . . . . 4 3 2 1 N/M N/A
- Understand the biologic basis for the investigation of immune checkpoint inhibitors in combination with chemoradiation therapy for patients with nonmetastatic NSCLC. . . . 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:

- 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. . . . . 4 3 2 1 N/M N/A
- Recognize immune-related adverse events and other common side effects associated with the use of immune checkpoint inhibitors as consolidation therapy for patients with Stage III NSCLC, and offer supportive strategies to minimize and/or manage these toxicities. . . . . 4 3 2 1 N/M N/A
- Recall the design of ongoing clinical trials evaluating novel therapeutic approaches for locally advanced 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
Andreas Rimner, MD	4 3 2 1	4 3 2 1
Corey J Langer, 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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