



Multidisciplinary Approaches to Cancer Symposium

Tumor Board: Management of Lung Cancers

Moderator: Arya Amini, MD

Panelists: Christine Lovly, MD, PhD & Dan J. Raz, MD, MAS

Panel & Disclosures

Arya Amini, MD

Associate Professor, Department of
Radiation Oncology
Section Chief, Thoracic and Skin
Radiation Oncology
City of Hope

- *Consultant for AstraZeneca, and Elsevier;
and Grant/Research Support from
AstraZeneca, Genentech, RefleXion, and
Varian*

Christine Lovly, MD, PhD, FASCO

Division Chief, Thoracic Medical Oncology
Professor, Department of Medical
Oncology & Therapeutics Research
Co-Director, Lung Cancer and Thoracic
Oncology Program
City of Hope

- *AbbVie, Amgen, AnHeart, Astra Zeneca, Black
Diamond, BMS, Boehringer Ingelheim,
Daiichi Sankyo, Exact, Foresight, Foundation
Medicine, Guardant, Genentech, Gilead,
Guardant, Immunity Bio, Jazz, JNJ, Merck,
Novartis, Nuvation, Onvivo, Pfizer,
Regeneron, Summit, Takeda, Taiho, Tempus*

Dan J. Raz, MD, MAS

Professor, Department of Surgery
Co-Director, Lung Cancer and Thoracic
Oncology Program
City of Hope

- *Grant/Research Support from AstraZeneca*

This presentation and/or comments will be free of any bias toward or promotion of the above referenced company or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.



Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.



Case 1: Stage IIIA Lung Adenocarcinoma

65yo woman with history of smoking

- **7/16/2025: 19mm RML nodule identified on LDCT for lung cancer screening**
- **9/30/2025: Robotic bronchoscopy with biopsy and EBUS showed**
 - Invasive nonmucinous adenocarcinoma, moderately differentiated with acinar architecture
 - EBUS: Level 4R=malignant cells, Level 7=benign
 - NGS testing= KEAP1, P53 mutations. PDL1 not performed due to inadequate tissue.
- **PMHx: COPD, CAD, DM2, HTN, HLD, Aortic stenosis**
- **Social History: smoked ½ pack per day x50 years, continues to smoke.**

Works in retail packing plant, walks regularly for work but does not exercise.
- **Family history: Sister died of lung cancer**



Work-up

Bain MRI 11/2025: No evidence of intracranial metastases.

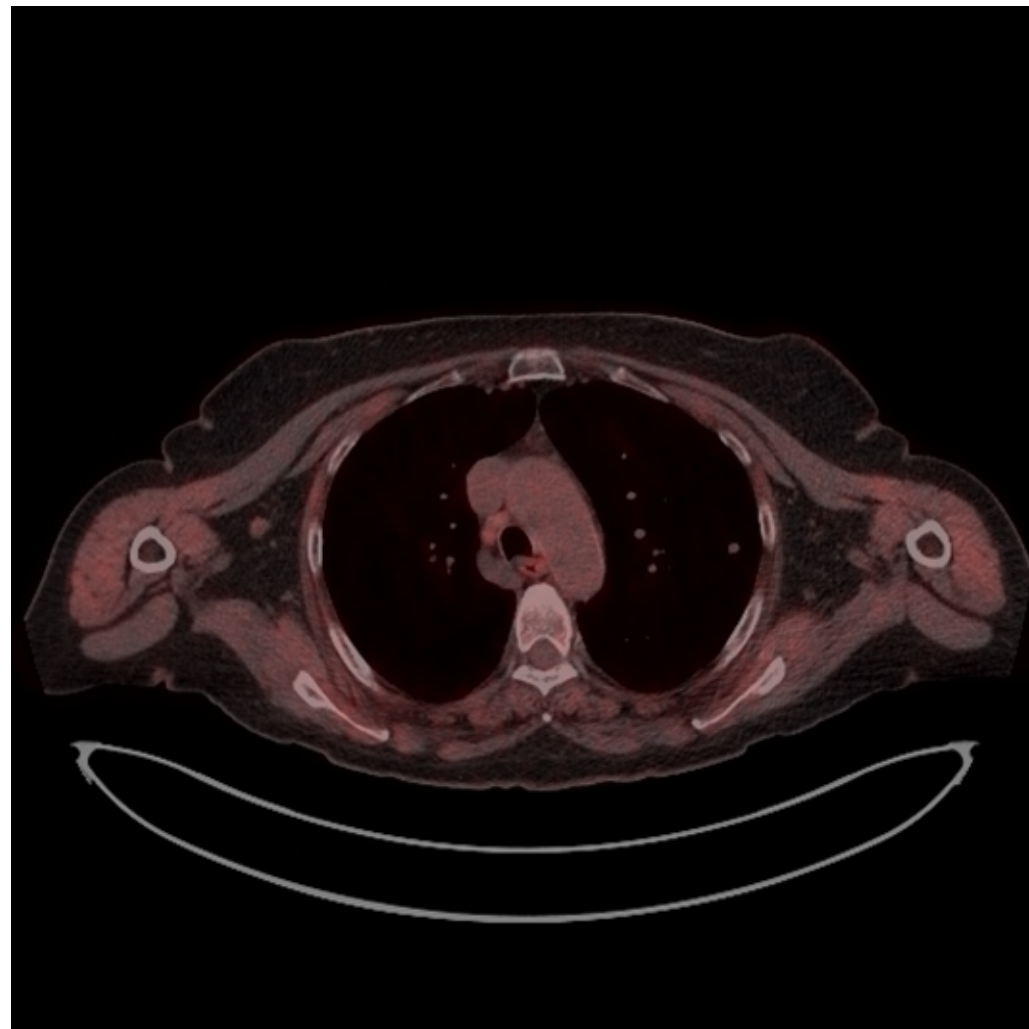
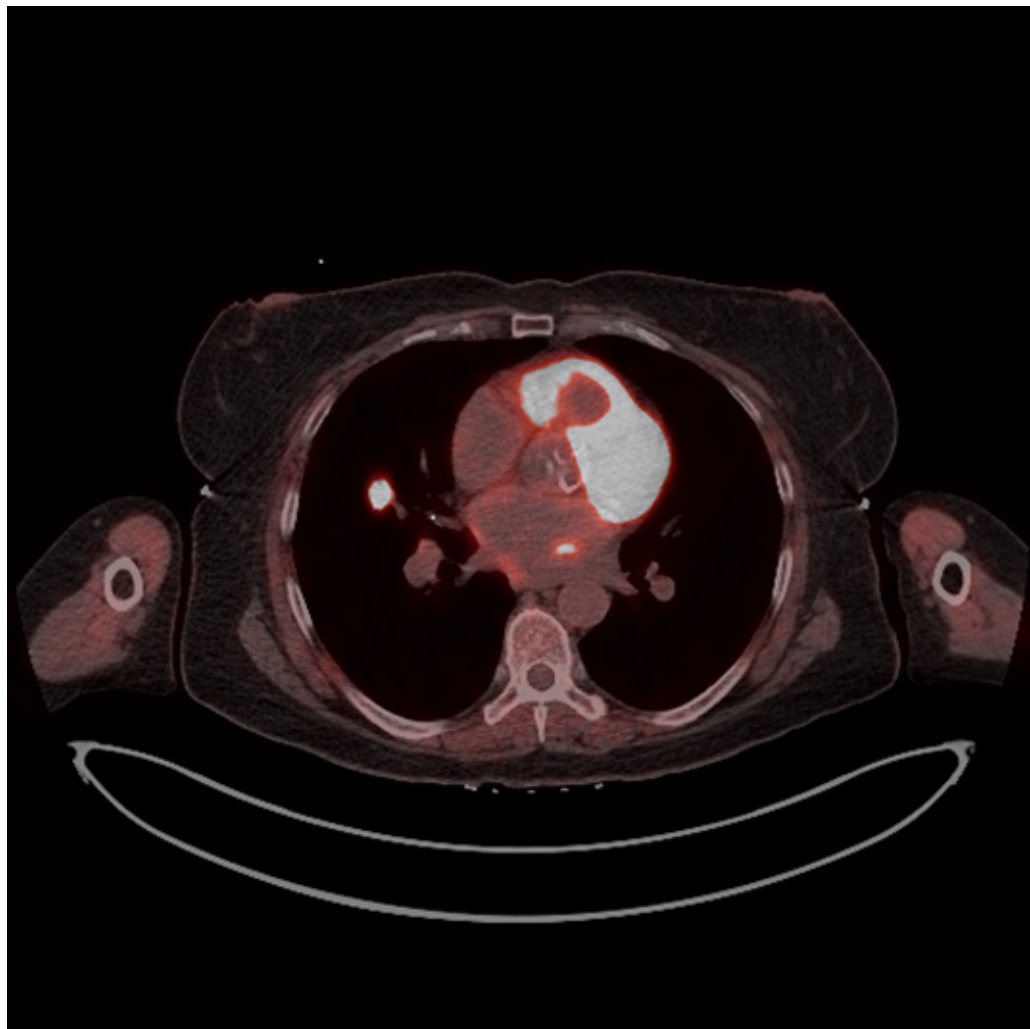
**PET/CT 12/2025: 2cm RML nodule SUV max 12.2; right paratracheal LN SUV 3.1
No evidence of distant metastatic disease.**

**Pulmonary function testing: FEV1 48% predicted, 61% post-bronchodilators;
DLCO 47% predicted.**

Mild dyspnea with stair climbing, but able to walk flat without difficulty.



Pretreatment PET/CT



Questions

Approach given poor pulmonary function

How to handle absence of PDL1 staining?

Treatment

- Initiated smoking cessation counseling. Declined medication.
- Initiated cisplatin/pemetrexed/nivolumab 1/28/2026 x 4 cycles, completed April 2026.
- Reimaging May 2026 showed RML nodule decreased to 7x4 mm.
- Underwent cardiac evaluation for pre-operative clearance
Found to have critical aortic stenosis
Underwent TAVR July 2026, rec aspirin for 3-6 months
- Repeated PFTs after smoking cessation May 2026: FEV 1 66% predicted, DLCO 46%.

Posttreatment CT



Surgery

- August 2026: Robotic RML lobectomy
Discharged home POD1
Required home oxygen with activity
- Pathology: No residual viable carcinoma (pCR)

Questions for discussion

- Was surgery the best option?
- Radiation therapy after induction chemo-IO when surgery is declined
- Should ICI therapy be continued when there is pCR?

Case 2: Oligometastatic EGFRmut NSCLC: Integrating Targeted Therapy and Local Consolidative Treatment

Patient Profile

- 62-year-old female
- Never smoker
- PMH: mild hypertension
- FH: No h/o lung cancer
- SH: Works as an office assistant
- ECOG PS: 0

Presenting Symptoms:

- Dry cough x 6 mo
- Mild dyspnea on exertion
- Unintentional 8lb weight loss

Diagnostic Workup

CT Chest

- 4.2 cm RUL mass
- Enlarged right hilar lymph nodes

PET/CT

- Primary lung lesion, SUV 12
- Right hilar and mediastinal lymph nodes
- Solitary left adrenal metastasis measuring 2.3 cm, SUV 10

Brain MRI

- Negative

Liquid Biopsy: EGFR exon 19 deletion, TP53 R273H

Tissue Biopsy: Lung adenocarcinoma, TTF1+

- ✓ PDL1 TPS 40%, MET IHC 3+ , 10%, HER2 IHC negative
- ✓ NGS: EGFR exon 19 deletion, TP53 R273H

Diagnosis:

- Stage IVB adenocarcinomaT2bN2bM1b (AJCC 9th edition)
- Single adrenal metastasis



Question

What is the preferred first-line treatment?



Treatment Course

Systemic Therapy

- Started on FLAURA2 regimen: Osimertinib plus Carboplatin (AUC 5) and Pemetrexed (500mg/m²)

Side Effect Monitoring

- Fatigue, but still able to work
- Mild nail bed changes

Response Assessments

- CT C/A/P prior to cycle 3 of carbo/pem plus osimertinib: (~6 weeks since therapy initiation)

RUL 4.2cm → 3.0cm

Mediastinal nodes: significant reduction

Adrenal metastasis: 2.3cm → 1.9cm

- CT C/A/P after 4 cycles of carbo/pem plus osimertinib (~12 weeks since therapy initiation)

RUL 4.2cm → 3.0cm → 2.1cm

Mediastinal nodes: significant reduction, not pathologically enlarged

Adrenal metastasis: 2.3cm → 1.9cm → 1.2cm

Questions

1. After completing 4 cycles of carboplatin/pemetrexed/osimertinib, what additional systemic treatment to pursue now?
2. Should local consolidative radiation be pursued?
 - If yes, what is the optimal timing of local consolidation therapy (LCT)?
 - In this case, what site(s)?
3. Is additional imaging needed now in consideration of LCT? Brain MRI? PET scan?

Summary table of osimertinib + local consolidation therapy

Regimen	Duration of Osi	Toxicities	PFS (time from Osi start) Median	OS Median
COH/UT SW: Osi+ consolidative RT	8-10 wks (1 st line)	Pneumonitis (5%) Dysphagia (15%)	32.3 mons	45 mons
NorthStar: NCT03410043 Osi+ consolidative local tx vs Osi	6-12 wks (1 st /2 nd line Osi)	Pneumonitis (10.7%, 1.8% G3) Skin (64%) Paronychia (58%)	25.3 mons vs 17.5 mons	N/A
LUNG-SORT (NCT04764214): 3rd gen TKI + RT (80% Osi, 20% almonertinib)	3.7 mons (median) before RT (1 st line EGFR TKI)	Pneumonitis (27.9%), esophagitis (26.2%)	29.9 mons	NR (2 yr OS 86.4%)

Treatment Course - Two Years Later

Patient Profile

- Patient remains on osimertinib, 80mg po qday
- ECOG PS 0
- Still working full time

Surveillance Imaging:

- Stable intrathoracic disease
- New 1.2cm isolated liver lesion

Liquid Biopsy: EGFR exon 19 deletion, TP53 R273H

Tissue Biopsy: Lung adenocarcinoma, TTF1+

- ✓ PDL1 TPS 5%, **MET IHC 3+ , 50%**, HER2 IHC negative
- ✓ NGS: EGFR exon 19 deletion, TP53 R273H

Questions

1. How to treat oligoprogression?
2. Is a change in systemic therapy needed at this time?
3. Are the biomarker studies informative?

Case 3A: Early-Stage, Node-Negative Disease

- 68-year-old, 40 pack-years, ECOG 0 — incidental 2.2 cm right upper lobe nodule found on lung cancer screening CT
- PET-CT: SUV 9.4 in the primary, no nodal or distant uptake. MRI brain negative
- Biopsy: small cell carcinoma, TTF-1 positive, synaptophysin positive, Ki-67 greater than 80%
- **Mediastinal staging (mandatory)**— EBUS or mediastinoscopy before committing to any local-therapy-alone plan. Occult nodal disease is common
- Final stage: cT1cN0M0, limited stage — this is the small minority of SCLC eligible for surgery or SBRT
- Surgery or SBRT? Systemic therapy after? Role of PCI?

Case 3A: Early-Stage, Node-Negative Disease

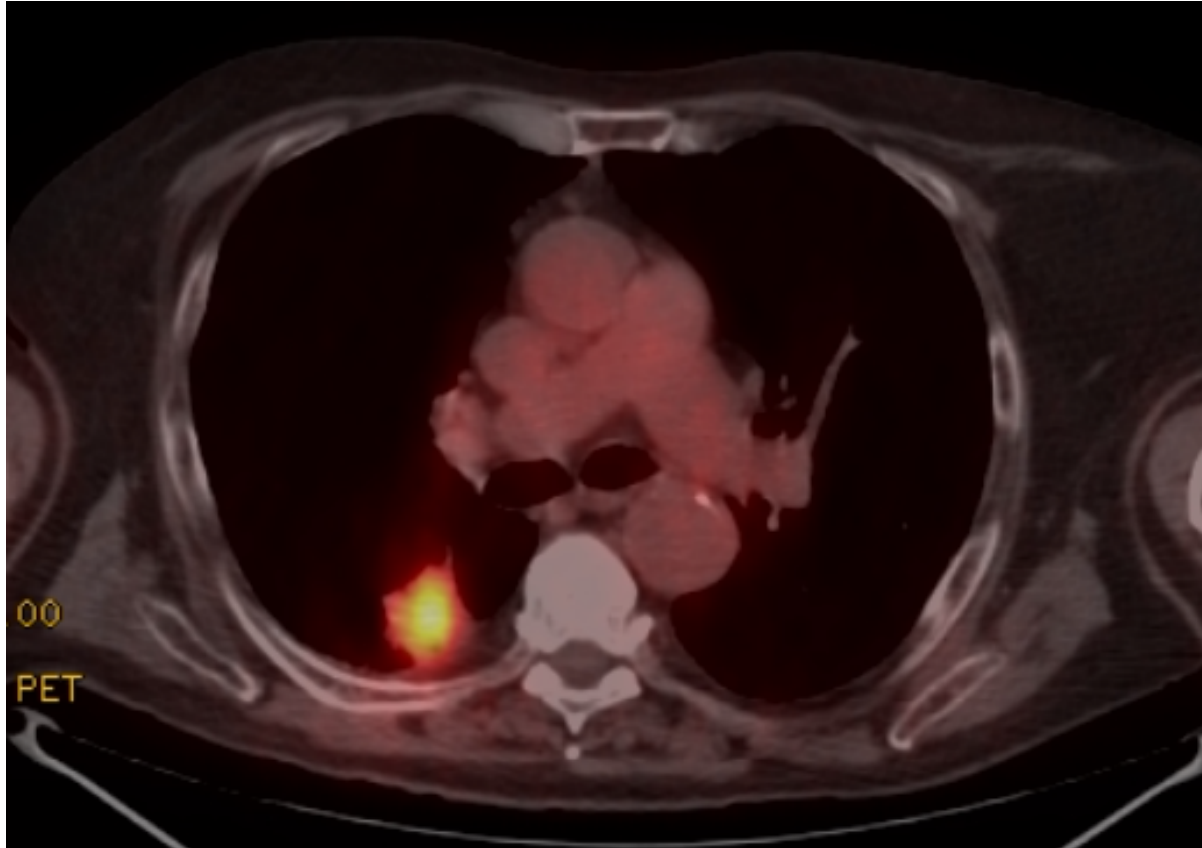


Figure 1. Fused PET/CT: 2.2 cm right upper lobe nodule, SUV max 9.4, with no nodal or distant uptake.

Imaging and Staging Findings

- **Primary lesion:** 2.2 cm spiculated right upper lobe nodule, peripheral location
- **SUV max 9.4**
- **No nodal or distant uptake;** MRI brain negative
- **PET cannot exclude occult N2 disease** — mediastinal staging with EBUS or mediastinoscopy is still required

Early Stage: Lobectomy versus SBRT

Surgery: Lobectomy

- **Candidates:** T1–2N0 only, pathologically node-negative, with adequate pulmonary and cardiac reserve
- **Lobectomy with systematic mediastinal nodal dissection** is the standard operation; sublobar resection only if physiologically forced
- **Adjuvant platinum/etoposide for 4 cycles is mandatory** regardless of margins — surgery alone is not curative therapy in SCLC
- **If nodes are positive on final pathology**, consider postoperative thoracic radiotherapy +/- chemotherapy
- **Outcomes:** resected stage I series report 5-year overall survival in the range of 50%, the best in the disease

SBRT: Medically Inoperable

- **Dose:** 50-60 Gy in 5 fractions or 54 Gy in 3 fractions to the peripheral primary; ultracentral consider 60 Gy in 8 fractions
- **Local control exceeds 90%** — the failure pattern is distant, not local, which is exactly why systemic therapy still matters
- **Adjuvant platinum/etoposide for 4 cycles???**
- **25-year institutional series** show comparable overall survival between surgery and SBRT in stage I when both are followed by chemotherapy, with selection bias caveats
- **Not appropriate** for any nodal disease — those patients belong on the chemoradiation pathway or larger tumors?

Case 3B: Patient decided not to proceed with treatment and follows up 6 months later with local progression

- 68-year-old, ECOG 1 — presents with cough and hyponatremia, sodium 126, from SIADH
- CT: 5.2 cm right lung mass with enlarged R hilar node
- PET suggests at least N1 disease with no distant sites; MRI brain negative. Additional mediastinal staging?
- Stage: cT3N0M0 —Treatment intent remains curative
- **Correct the hyponatremia first:** fluid restriction and tolvaptan as needed. SIADH typically improves rapidly with effective systemic therapy
- **Key decision:** treatment plan and timing of radiation and chemotherapy? When do we start immunotherapy?

Case 3B: Limited Stage

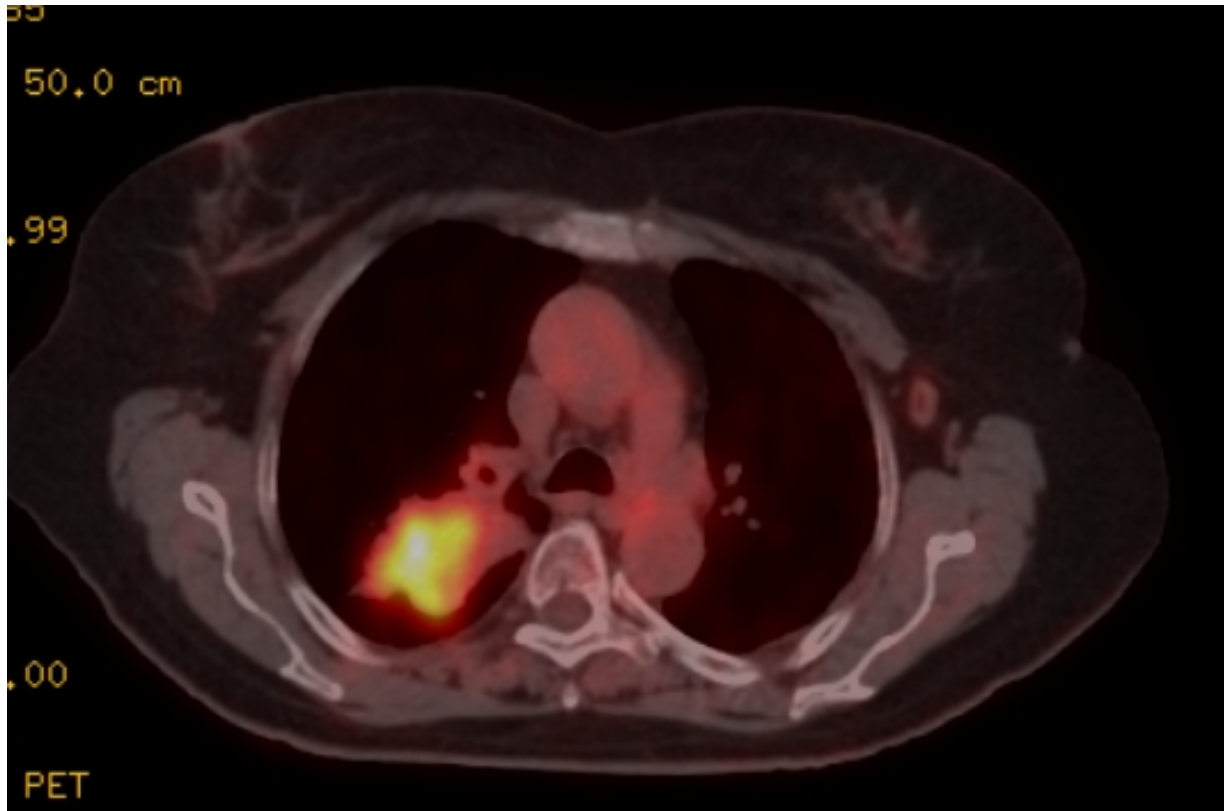


Figure 1. Fused PET/CT: 5.6 cm right upper lobe nodule, SUV max 13.6, with mild hilar node uptake (SUV 3.7)

Imaging and Staging Findings

- **Primary lesion:** 5.6 cm spiculated right upper lobe nodule, peripheral location (**SUV max 13.6**)
- **N1 nodal disease?** (**SUV max 3.7**)
- **No distant uptake;** MRI brain negative
- **PET cannot exclude occult N2 disease** — mediastinal staging with EBUS is still recommended

Final Diagnosis

A. LYMPH NODE, STATION 7, EBUS GUIDED FINE NEEDLE ASPIRATION:

- Negative for metastatic malignancy.
- Lymphoid cells are present with ciliated bronchial cells, consistent with a lymph node sampling.
- Cell block concurs with smear findings.

B. LYMPH NODE, STATION 11R, EBUS GUIDED FINE NEEDLE ASPIRATION:

- Negative for metastatic malignancy.
- Lymphoid cells are present with ciliated bronchial cells, consistent with a lymph node sampling.
- Cell block concurs with smear findings.

C. LYMPH NODE, STATION 4R, EBUS GUIDED FINE NEEDLE ASPIRATION:

- Negative for metastatic malignancy.
- Lymphoid cells are present, consistent with a lymph node sampling.
- Cell block concurs with smear findings.

D. LYMPH NODE, STATION 4L, EBUS GUIDED FINE NEEDLE ASPIRATION:

- Negative for metastatic malignancy.
- Lymphoid cells are present, consistent with a lymph node sampling.
- Cell block concurs with smear findings.

E. LYMPH NODE, STATION 11L, EBUS GUIDED FINE NEEDLE ASPIRATION:

- Negative for metastatic malignancy.
- Lymphoid cells are present, consistent with a lymph node sampling.
- Cell block concurs with smear findings.

Concurrent Chemoradiation: Regimen, Dose, and Timing

Systemic Backbone and Timing

Cisplatin/etoposide for 4 cycles is the backbone; substitute carboplatin for renal impairment or neuropathy concerns

Start radiation ideally with cycle 1 or 2 — delayed radiation impacts OS

Concurrent beats sequential in every comparison; reserve sequential delivery for patients who cannot tolerate combined therapy

Management of adverse events including esophagitis – plan nutritional support proactively; early-intervention (Magic mouthwash, narcotics, steroids, PPI)

Restage 4 to 6 weeks after completion to assess response and eligibility for consolidation

Radiation Dose and Fractionation

45 Gy in 30 fractions twice daily over 3 weeks remains the reference regimen

CONVERT found no superiority for 66 Gy once daily over 45 Gy twice daily; both are acceptable, and long-term follow-up confirms durable outcomes in each arm

High-dose twice daily, 60 Gy in 40 fractions (phase 2 data), improved overall survival in a subsequent randomized trial and is reasonable at experienced centers

Practical reality: twice-daily delivery is more effective? (NRG-LU005) but logistically demanding for patients and departments

Modern planning with IMRT, involved-field nodal targeting, and PET-based volumes has meaningfully reduced esophagitis and pneumonitis

Timing Is Everything: NRG LU005 versus ADRIATIC

NRG LU005: Concurrent Atezolizumab

- **Design:** phase III, atezolizumab given concurrently with chemoradiation and then continued as maintenance
- **Result: negative.** Concurrent atezolizumab did not improve overall survival versus standard chemoradiation alone
- **Why it likely failed:** concurrent checkpoint blockade may blunt the radiation-induced immune priming rather than amplify it, and adds toxicity during the most intensive phase of therapy
- **Important secondary finding:** twice-daily radiation conferred better survival than once-daily radiation, reinforcing the twice-daily regimen
- **Practice impact:** do not give immunotherapy concurrently with chemoradiation in limited-stage disease outside a trial

ADRIATIC: Consolidation Durvalumab

- **Design:** phase III, durvalumab started as consolidation only after chemoradiation was completed, in patients without progression
- **Result: positive.** Median overall survival 55.9 versus 33.4 months, a 22.5-month gain, with progression-free survival improved by 7.4 months
- **Why it worked:** sequencing immunotherapy after radiation lets the antigen release and immune priming from chemoradiation occur first, then sustains the response
- **Benefit was consistent** across once-daily and twice-daily chemoradiation regimens and regardless of prophylactic cranial irradiation
- **Practice impact:** consolidation durvalumab after chemoradiation is the current standard of care in limited-stage disease
- **How to deliver it:** restage 4 to 6 weeks after chemoradiation, confirm no progression, then start durvalumab. Watch for pneumonitis overlapping with recent thoracic radiation

Prophylactic Cranial Irradiation: Pros and Cons

Pros

- **PCI 25 Gy in 10 fractions** in patients with any response to first-line therapy roughly halves the incidence of brain metastases
- **Showed an overall survival benefit** in the landmark meta-analysis and in the extensive-stage EORTC trial
- **Strongest argument in limited stage** for patients in complete or near-complete remission being treated with curative intent
- **Choose PCI when MRI is not realistic:** if access, adherence, or reliable follow-up is in doubt, PCI is the safer choice
- **Hippocampal-avoidance PCI** plus memantine reduces neurocognitive cost while preserving the CNS benefit

Cons

- **The evidence base is dated:** the founding trials predate routine brain MRI – we were treating occult disease?
- **No benefit in the modern era:** the Japanese randomized trial in extensive stage found no survival benefit for PCI over MRI surveillance, and numerically favored surveillance
- **Surveillance performs equally well:** a meta-analysis of 14 studies and 2,881 patients found comparable overall survival and progression-free survival with active MRI surveillance
- **Real neurotoxicity cost:** measurable decline in memory and executive function, plus fatigue and alopecia
- **Often avoidable:** commit to brain MRI every 3 months for 2 years and PCI can be safely omitted. Decide before treatment ends and document the shared decision

MAVERICK (SWOG S1827), the randomized phase III trial of MRI surveillance alone versus MRI surveillance plus PCI: results presented at WCLC showed MRI surveillance alone had improved cognitive failure-free survival with no difference in OS

Case 3C: Relapse as Extensive Stage

- 14 months after chemoradiation, the same patient returns with fatigue, right upper quadrant pain, and new back pain
- Restaging: multiple hepatic lesions, an L3 vertebral body metastasis, and new contralateral lung nodules
- MRI brain: two sub-centimeter asymptomatic lesions
- Rebiopsy the liver lesion — confirms recurrent small cell
- This is now extensive stage: intent shifts from cure to durable disease control and symptom management
- Next steps in treatment – any additional information needed? Systemic therapy? Radiation?

Extensive Stage: First-Line Chemoimmunotherapy

Systemic Therapy

Standard of care: platinum/etoposide plus a PD-L1 inhibitor for 4 cycles, then maintenance immunotherapy

IMpower133 established carboplatin/etoposide plus atezolizumab; CASPIAN established platinum/etoposide plus durvalumab. Both showed a significant overall survival benefit over chemotherapy alone

Absolute gains are modest, roughly 2 to 3 months in median survival, but with a meaningful long tail of durable responders

For this platinum-sensitive relapse, platinum rechallenge combined with immunotherapy is appropriate

Assess response every 2 cycles — SCLC responds fast, and early progression changes the plan quickly

Role of Radiation

Consolidative thoracic radiation per the CREST trial, 30 Gy in 10 fractions after chemotherapy response: no primary overall survival benefit at 1 year, but improved 2-year survival and significantly reduced intrathoracic progression

AIO-TRK-0320 (phase 2): TRT added to atezolizumab with higher adverse events impacting OS

RAPTOR trial pending

Best candidates are patients with residual thoracic disease and a good response at distant sites

Brain metastases: SRS vs whole brain

Palliative radiation for painful bone metastases, cord compression, or symptomatic airway obstruction

Surveillance: brain MRI every 3 months through treatment

Relapsed Disease: Second Line and Beyond

Second Line

Platinum-sensitive, more than 6 months: rechallenge with platinum/etoposide is reasonable

Lurbinectedin — phase 2 basket trial showed a 35.2% response rate, median progression-free survival 3.5 months, median overall survival 9.3 months, with better outcomes in the platinum-sensitive subset

Topotecan remains an option but carries a meaningfully worse toxicity profile

Third Line and Beyond

Tarlatamab, a DLL3-directed bispecific T-cell engager — DeLLphi-301 showed a 40% response rate, median progression-free survival 4.9 months, and median overall survival 14.3 months after 2 or more prior lines, with 55% of responses ongoing at data cutoff

Requires monitored step-up dosing for cytokine release syndrome and neurotoxicity

Offer clinical trial enrollment

Thank You

cityofhope.org

