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*Accredited Educational Activities for  
Advanced Practitioners in Oncology*

# **Collaborative Practice in the Management of Patients With Cancer**

**Use of Diagnostic Tests in  
Advanced Non-Small Cell Lung Cancer:  
Skills Presentation**

# Program Chair

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# Disclosures

## Faculty

**Ms. Eaby-Sandy** has acted as a consultant for AstraZeneca and Clovis; she has served on speakers bureaus for Amgen, Celgene, Eisai, and Merck.

## Planning Committee

Moshe C. Ornstein, MD, MA, Cleveland Clinic Taussig Cancer Institute (Reviewer) has nothing to disclose. Alana Brody, Terry Logan, Lynn Rubin, and Wendy Smith (MEI) have nothing to disclose. Sandra Leatherman, Annamarie Luccarelli, and Jessica Tamasi (APSHO) have nothing to disclose. Claudine Kiffer and Annie Yueh (Harborside Press) have nothing to disclose.

# Learning Objectives

- Demonstrate a foundational understanding of how to interpret imaging studies that are used in the management of NSCLC
- Choose relevant molecular/biomarker tests to identify the most appropriate therapy for the patient with NSCLC (e.g., targeted or immunotherapy)
- Use appropriate management strategies for toxicities associated with targeted therapies
- Differentiate between the various treatment options available for NSCLC: Comparing mechanisms of action, toxicity profiles, and monitoring
- Manage toxicities associated with different agents used to treat NSCLC
- Demonstrate an understanding of the science behind immune checkpoint inhibition and how this drug category differs from other available and evolving options for NSCLC, including cytotoxic chemotherapy

# Objectives

Review the following (all with respect to lung cancer):

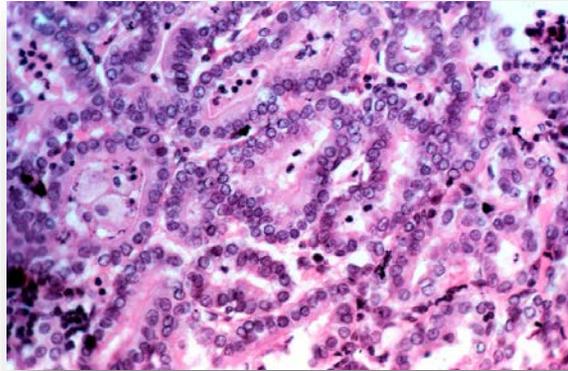
- Pathology reports
- Molecular lab results
- Radiology interpretation
- CT chest interpretation
- PET/CT interpretation

# PATHOLOGY REPORTS

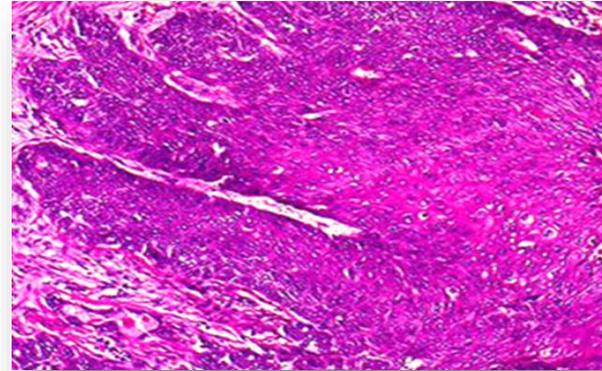
# Case Study #1

- KB is a 31-year-old female smoker who presents to clinic for evaluation of her stage IV NSCLC
- She underwent bronchoscopy for biopsy of a LLL tumor

# Histologic and Molecular Differentiation Determines Therapeutic Decision-Making



Adenocarcinoma



Squamous

## Issues:

- Biopsies for histology vs. FNAs for cytology ( $\pm$  cell blocks)
- More tissue is better than scanty samples
- Experience of pathologists<sup>1</sup>
- Use of special stains
- Molecular profiles

# Staining Patterns for NSCLC

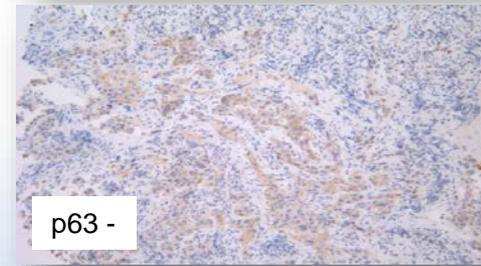
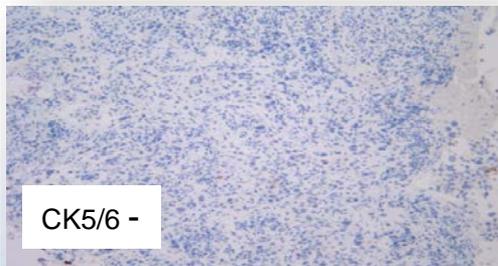
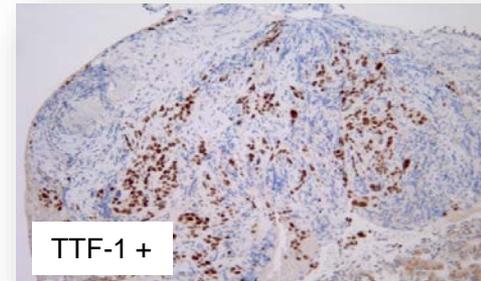
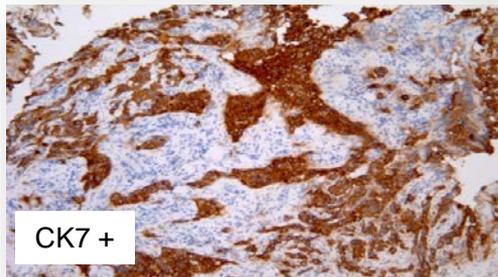
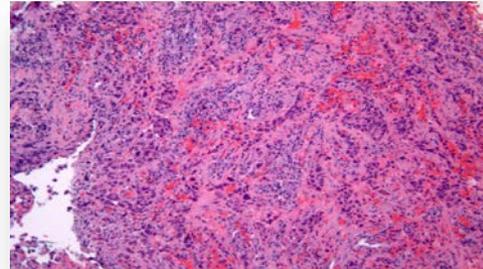
Five common IHC stains used to classify a NSCLC to get a histopathologic diagnosis:

- TTF-1
- P63
- CK5/6
- CK7
- CK20

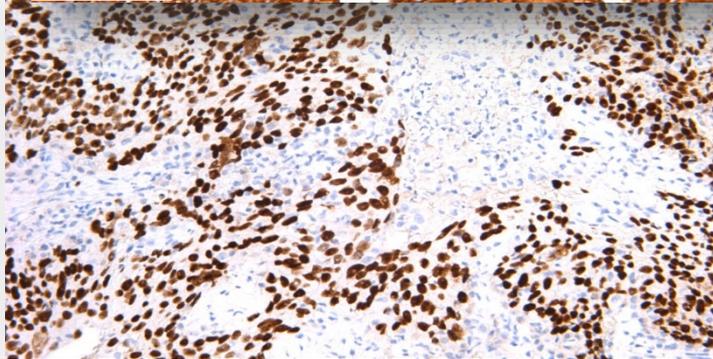
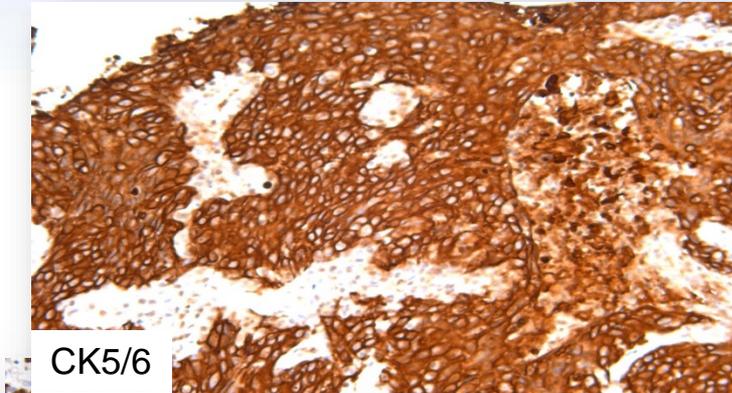
# IHC Staining in NSCLC

	TTF-1	p63	CK5/6	CK7	CK20	Comments
NSCLC, favor adeno	+	–	–	+	+/-	Could have weak p63
NSCLC, SCC	–	+	+	–	–	Strong + p63, negative others
NSCLC, adenosquamous	+	+	+	+	–	
NSCLC, NOS	–	–	–	+	–	Compatible with pulmonary origin, if clinically consistent
Adeno, colorectal primary or pulmonary primary with intestinal phenotype	–	–		+/-	+	Stains cannot differentiate the two, clinical correlation required

# Pulmonary Adenocarcinoma



# Squamous Cell Carcinoma



- Typical IHC profile of SCC
  - CK5/6, p63 (crisp nuclear staining), and calretinin positive
  - TTF-1 negative

# Case Study #1 (continued)

- KB has a pulmonary adenocarcinoma; however, she is young, at risk for a mutation
- Should test all pulmonary non-squamous or NOS histology patients for minimum ALK rearrangements and EGFR mutations, which are actionable. NCCN does not recommend ROS1, which is rare, however, there is approved agent for this as well, so should be considered
- Consider testing patients with squamous NSCLC who are never smokers for ALK rearrangements and EGFR mutations.
  - Also can consider testing when small biopsy specimen or mixed histology.
- Larger panel (i.e., Next Gen Sequencing, CPD) are nice to have for evaluation for clinical trials

# MOLECULAR LAB REPORTS

# Molecular Pathology

- Most NSCLC samples are feasible to test for genotyping/molecular alterations
  - Bone biopsies usually not due to decalcification
  - Small percutaneous biopsies sometimes insufficient
- ALK, ROS1, RET are FISH tests
- Most of the rest require DNA extraction

# Liquid Biopsy

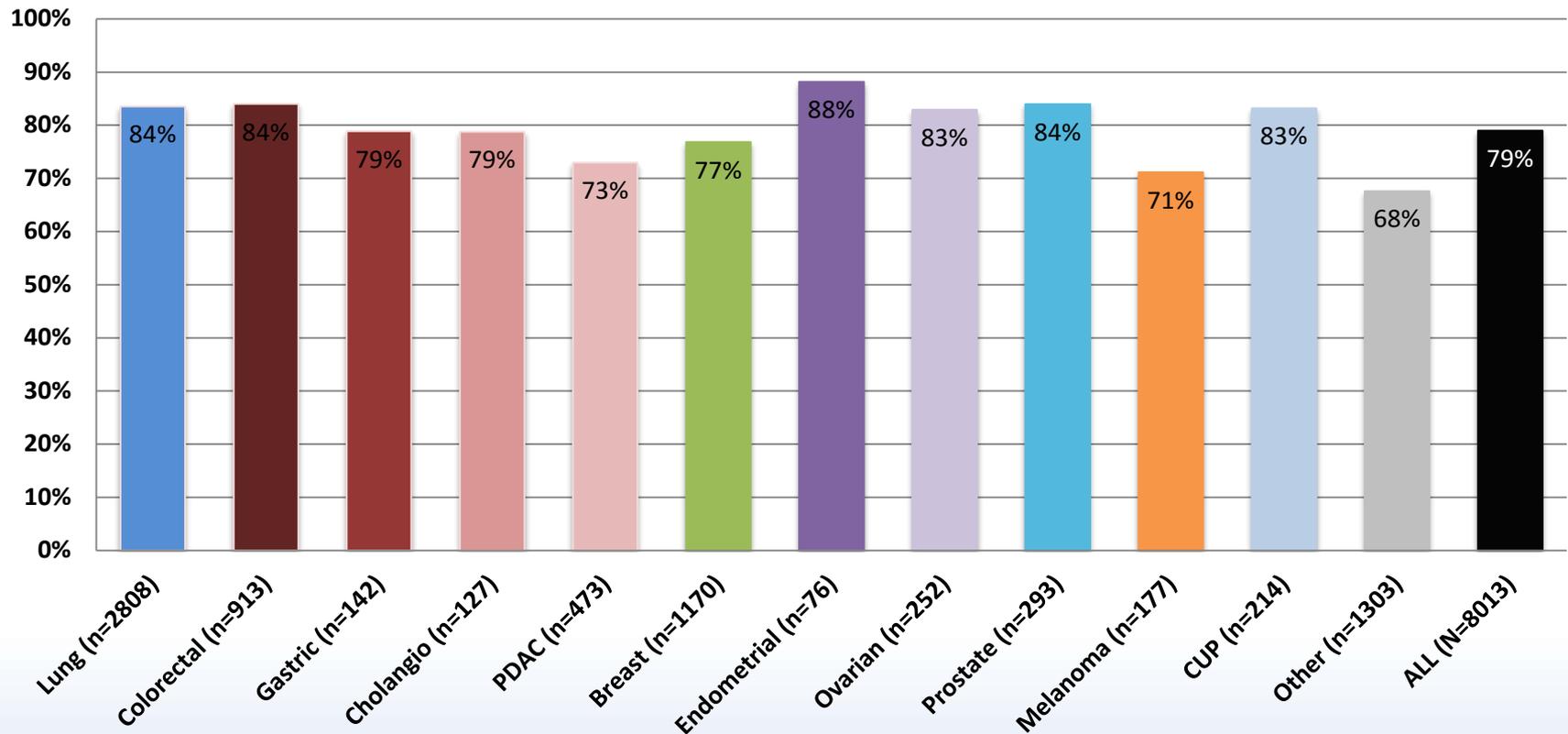
## Pros

- Does not require invasive procedure
  - Especially when looking for T790M
- Quick 2-week general turnaround
- Sensitivity good

## Cons

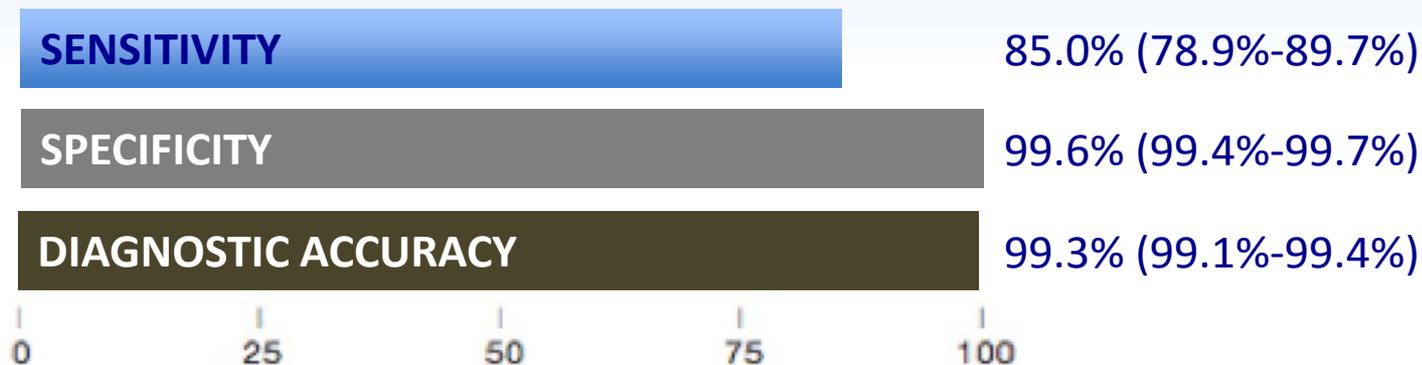
- Needle stick
- Cost to patient out of pocket
- Sensitivity not 100%
- Must collect and send via Fed Ex to company in timely fashion
  - Takes some lab coordination

# ctDNA Identified in Majority of Advanced-Stage Solid Tumor Cases (n = 9000)

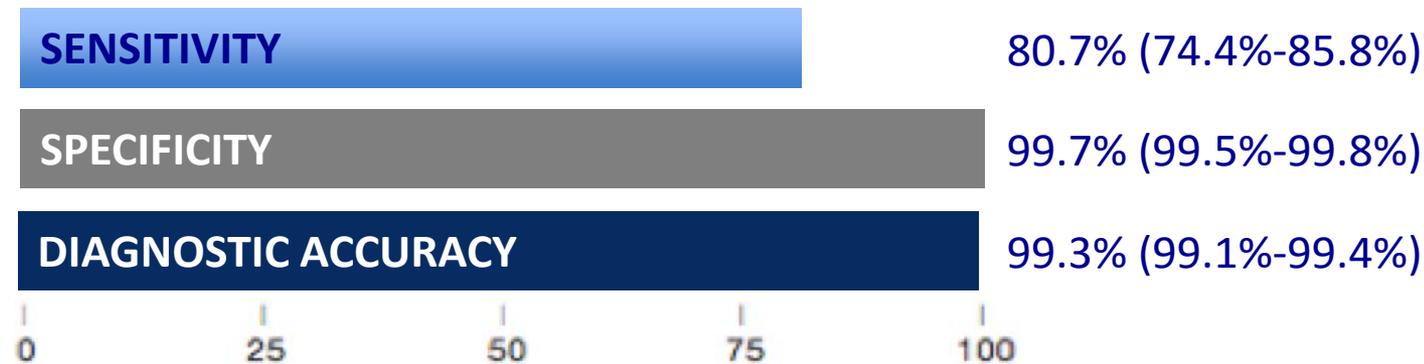


# Tissue NGS vs. Plasma Cell-Free NGS on 165 Paired Samples From 5 Centers

## Cell-free DNA vs. Tissue NGS



## Tissue vs. Cell-free DNA NGS



- Cell-free DNA sensitivity may be limited when tumor DNA is not shed into circulation.
- Tissue DNA sensitivity may be limited because samples fail to capture tumor heterogeneity.
- All sequencing (both tissue and cfDNA) on Illumina HiSeq 2500.

# Association Between Tissue vs. Plasma Genotyping Looking for T790M

- Study specific to NSCLC, primarily looking at T790M
  - A subset of patients that would require rebiopsy
- The sensitivity for detection of T790M in plasma was 70%
- Of the patients with T790M negative tissue biopsy, plasma detected a T790M mutation in 31% of them
- It is reasonable to start with plasma genotyping; if negative, proceed with tumor tissue biopsy

# RADIOLOGY INTERPRETATION

# Case Study #2

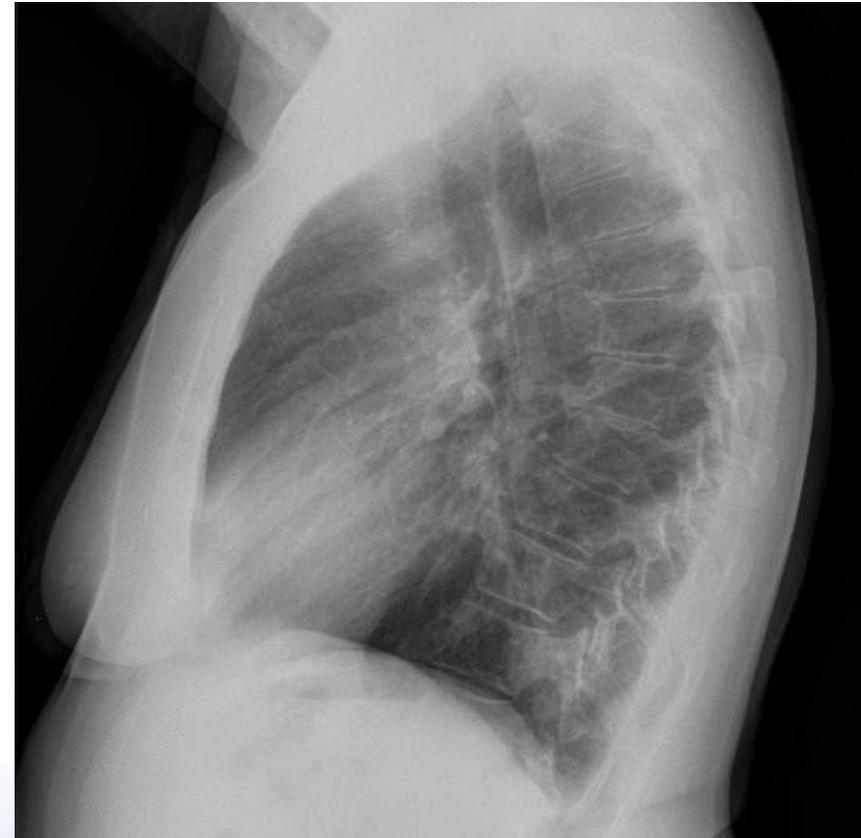
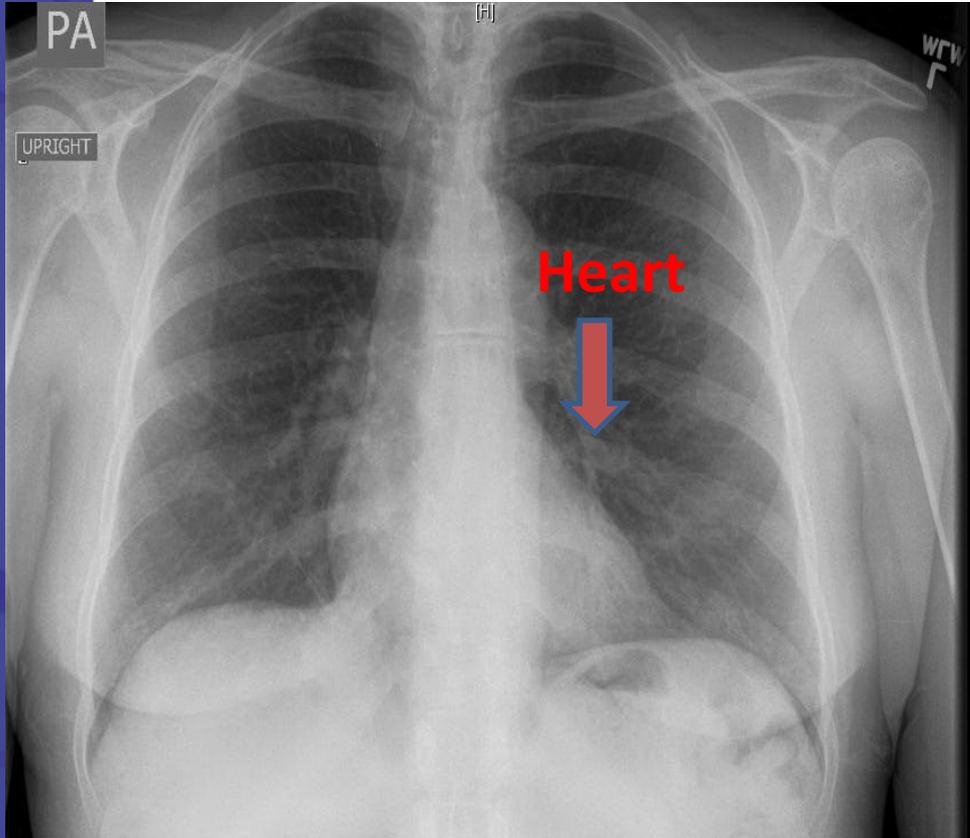
- JO is a 58-year-old man who works per diem jobs for the carpenter's union. He does not have insurance and rarely goes to the doctor.
- He smokes a pack a day of cigarettes and in January 2016 developed a cold and a wheeze that wouldn't go away with OTC medication.
- PMH only significant for non-Hodgkin's Lymphoma in 1988 treated with radiation only. And femur fracture with rod placed in 1965.
- CXR performed in ER followed up by a CT chest



# Chest X-Ray

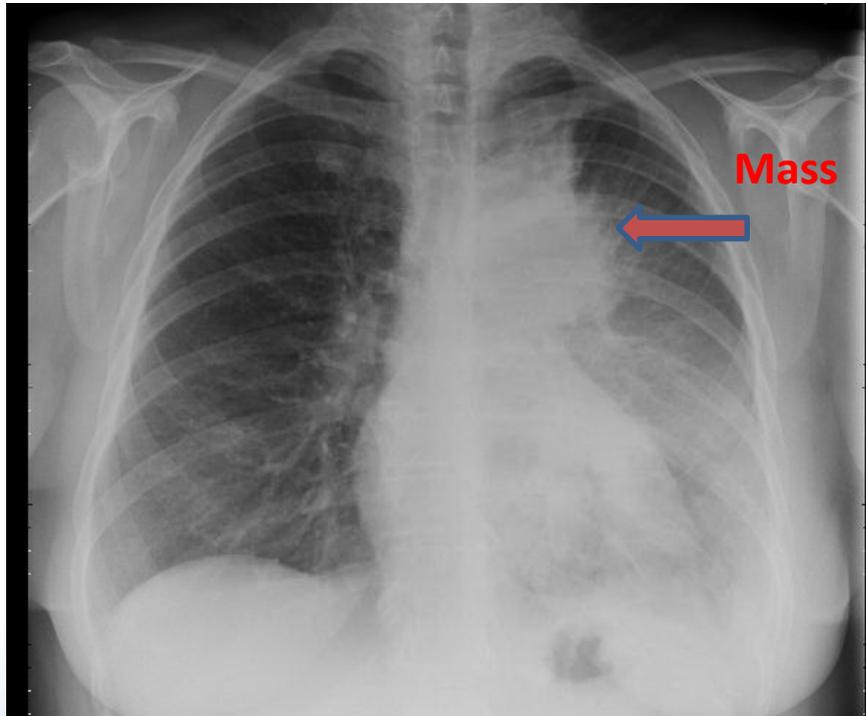
Posterioranterior (PA)

Lateral (always L sided)



# Mass vs. Pneumonia

## Mass LUL



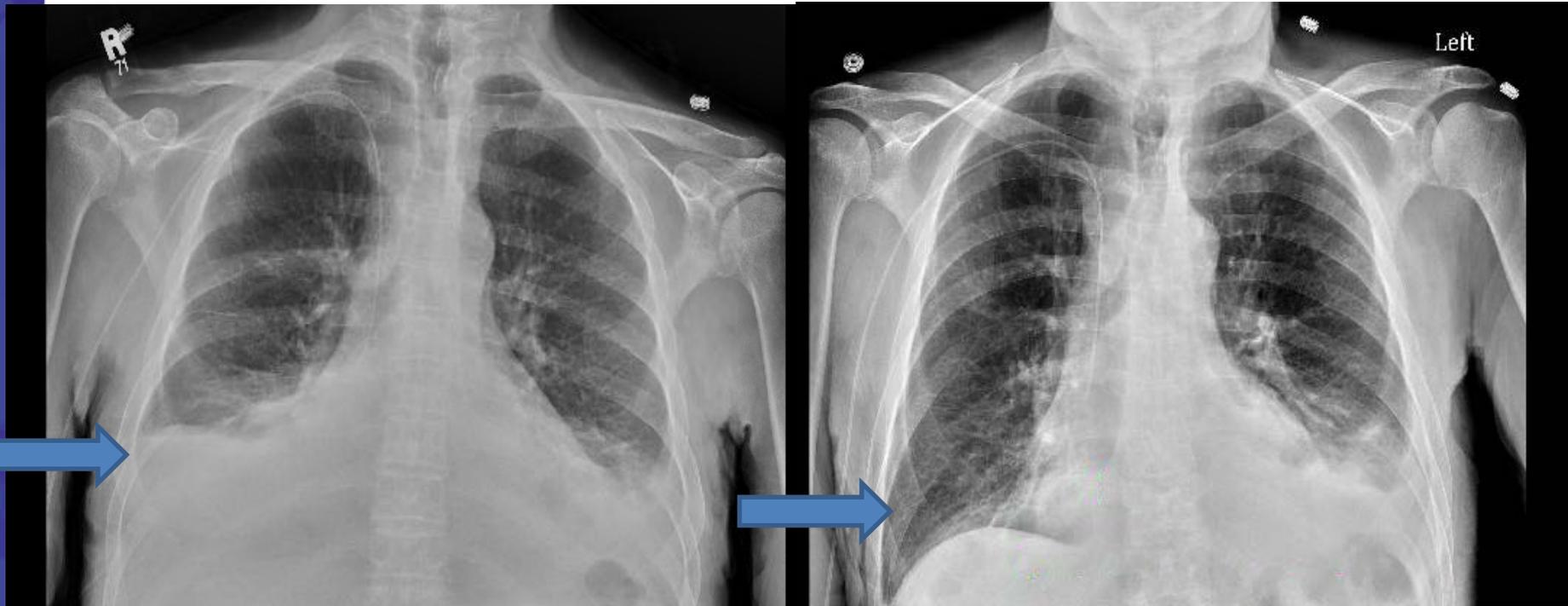
## Pneumonia/ Air space disease



# Pleural Effusion

Right-side pleural effusion

1 day after drained



# CT SCAN IMAGING

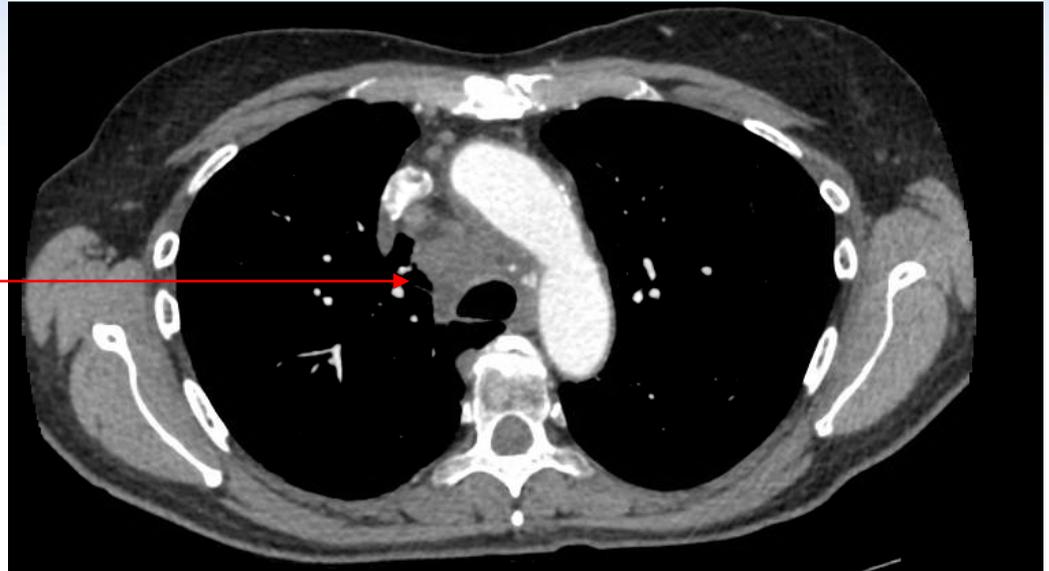
# Case Study #2 (continued)

- JO CT chest just following the CXR
- Note large RLL mass, surrounding and pinching off airways
- On chest/abd windows, note the large R hilar lymph node



# Mediastinal Lymphadenopathy

Large 2.5-cm  
malignant  
mediastinal lymph  
node



Normal-looking  
mediastinum



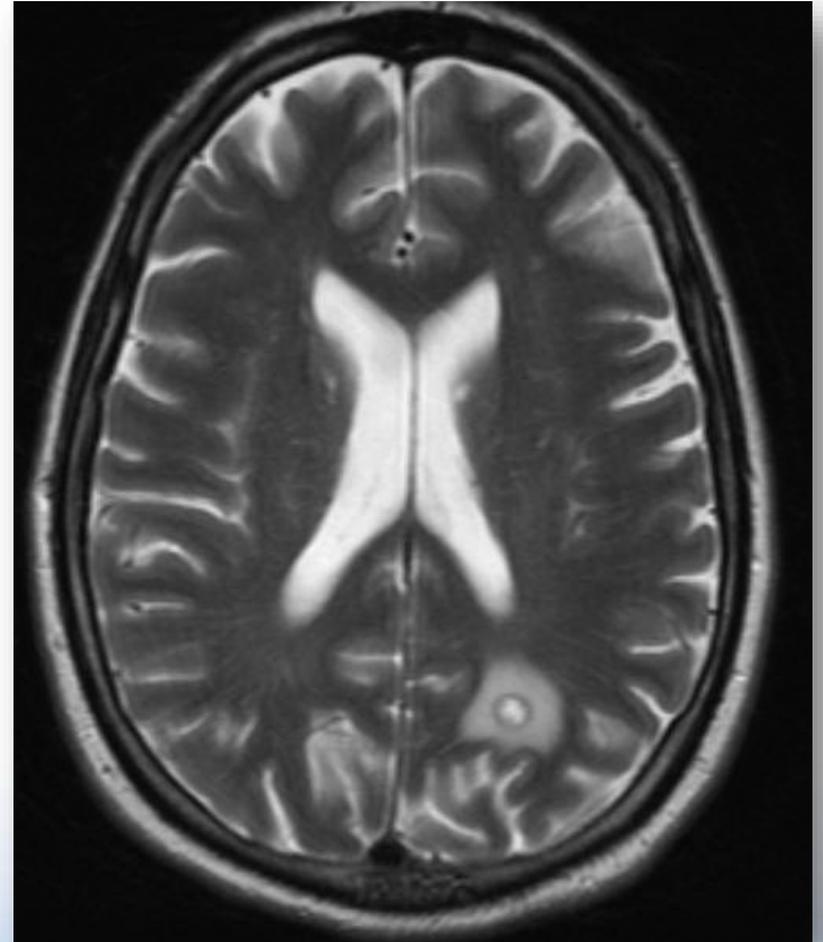
# Case Study #2 (continued)

- JO's CT chest continues down through the upper abdomen
- Liver looks WNL
- Note the R thickened adrenal gland
- Note on the PET fusion image, the light up in R adrenal, but also L adrenal FDG avid as well



## Case Study #2 (continued)

- JO also gets his baseline MRI brain
- Note the L parietal met with edema, 8 mm



# Case Study #1 (continued)

- KB is a 31-year-old female smoker who presents to clinic for evaluation of her stage IV NSCLC adenocarcinoma in 2010.
- Molecular testing at that time for EGFR, KRAS, and ALK showed no mutations, so she went on to receive chemotherapy.
- Two years later, after on and off of chemotherapy, radiation, we repeat a larger molecular panel to detect any abnormalities.

# Case Study #1 (continued)

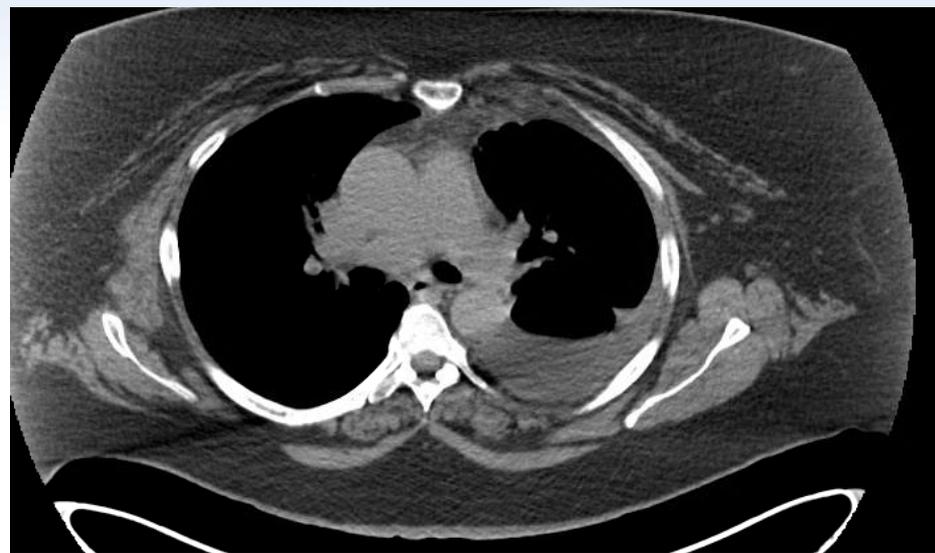
- An EML4-ALK gene translocation is discovered on her 2nd molecular test, and she now begins treatment with crizotinib 250 mg twice a day.
- About 3 weeks after starting drug, she calls the nurse practitioner and reports a new onset of shortness of breath and cough, no mucus.

# Interstitial Lung Disease

- About 3% of cases in crizotinib, 0.5% fatal
- On imaging study, will appear classic look like a cloudy disseminated, bilateral appearance
- Should rule out a pulmonary embolism, though if patient on a drug known to cause ILD, this would remain high on differential
- Can be termed pneumonitis as well

# Pleural Effusion on CT Chest

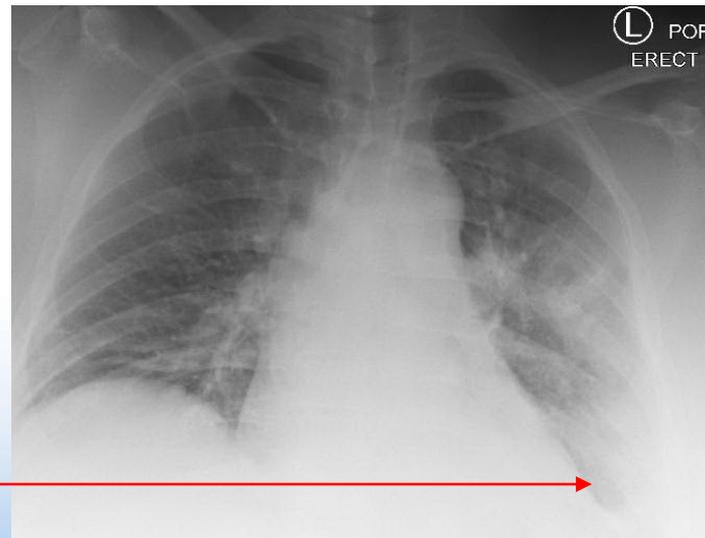
This is a 46-year-old obese female with EGFR mutation-positive metastatic NSCLC with L pleural effusion



CXR same day as CT scan

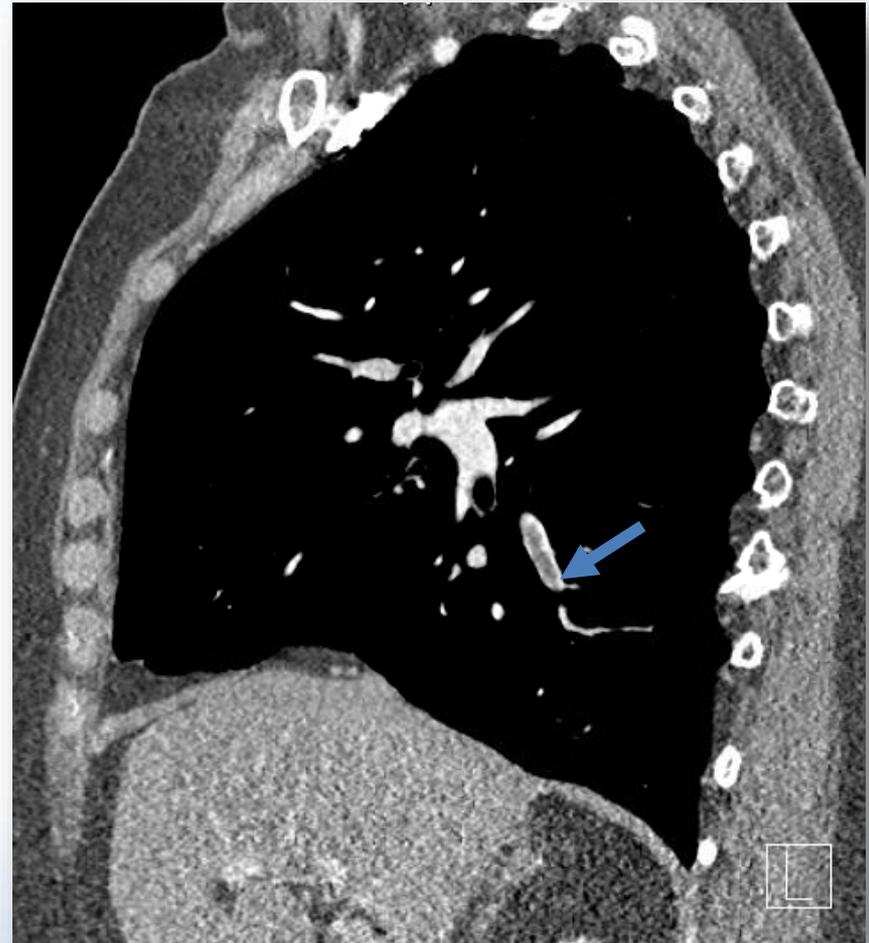
Pre-drainage

Postdrainage



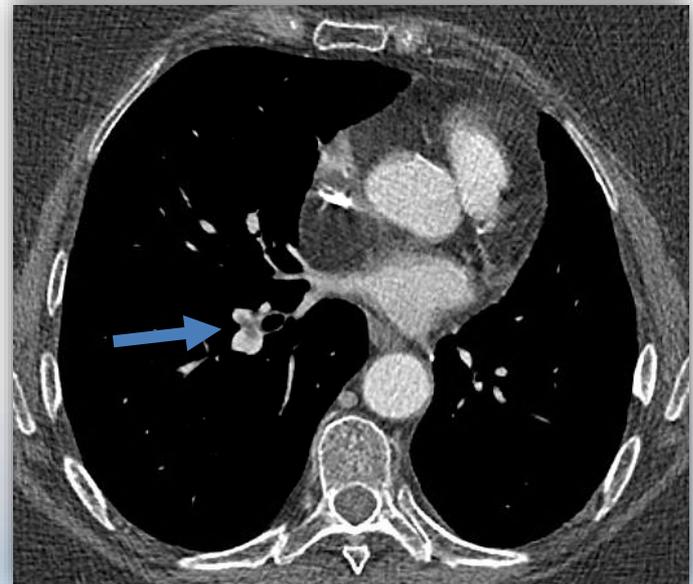
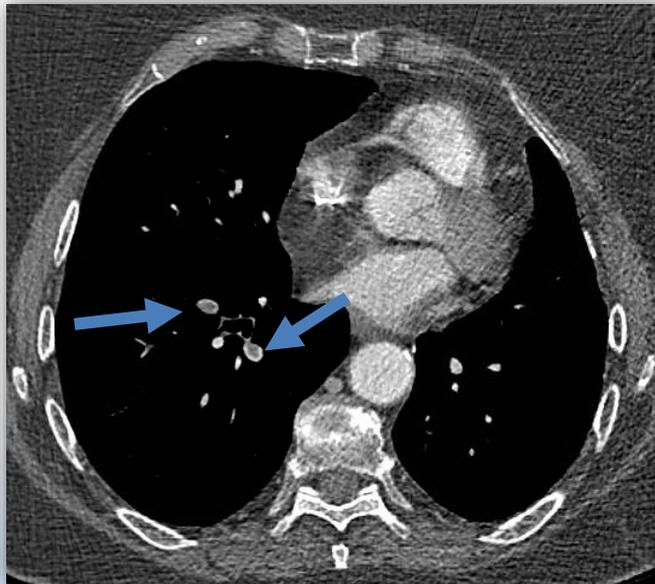
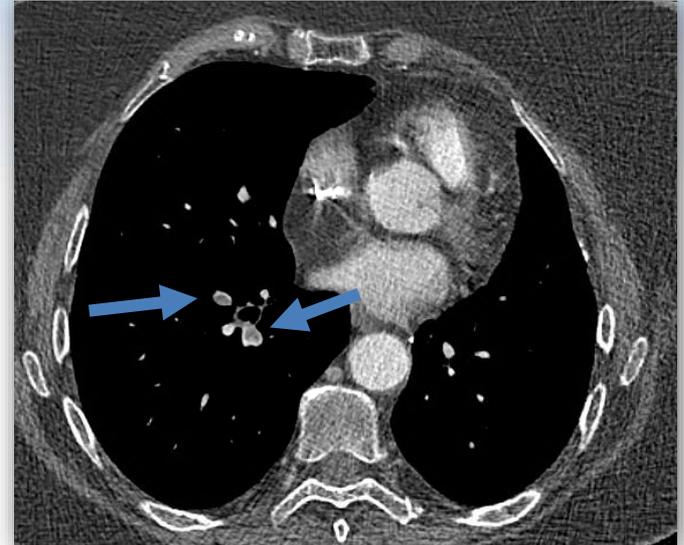
# Pulmonary Embolism

- Will see a filling defect in a vessel
- PE protocol CT chest very thin slices to look
- This was a routine CT chest on a stage III NSCLC patient who was not symptomatic
- Lateral views show it well



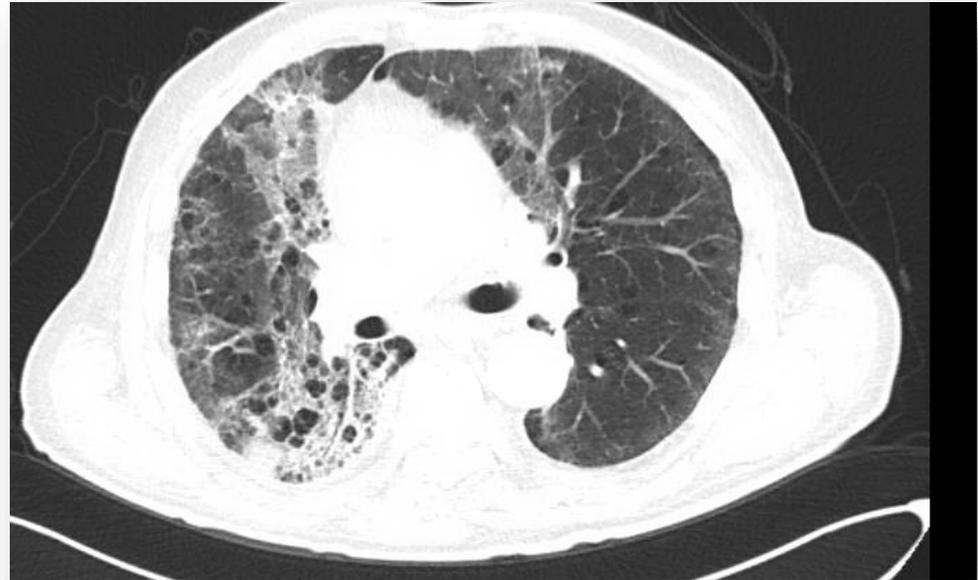
# Pulmonary Embolism (cont.)

- Same patient as last slide, these are the horizontal slices showing clot in the vessels.
- This can be difficult to see, I rely on radiologist's trained eye. If suspected, I personally speak with radiologist.



# Radiation Pneumonitis

- This was a 72-year-old former smoker with stage IIIA NSCLC, who had chemo/radiation
- 5 weeks after completing radiation developed SOB and dry cough
- Note linear appearance, not consolidative, unilateral



# Conclusions

- Pathology
  - IHC staining to identify NSCLC histology
  - Most specimens now able to suffice for molecular analysis, though bone rarely sufficient
  - Liquid biopsy may be less invasive and largely accurate
- Radiology interpretation
  - Numerous complications that arise in the lungs
  - APs must be able to at least identify the obvious complications on CXR and CT and act on these
  - When in doubt, call radiologist to discuss
  - Practice reading scans