


Lung Cancer Update for Primary Care

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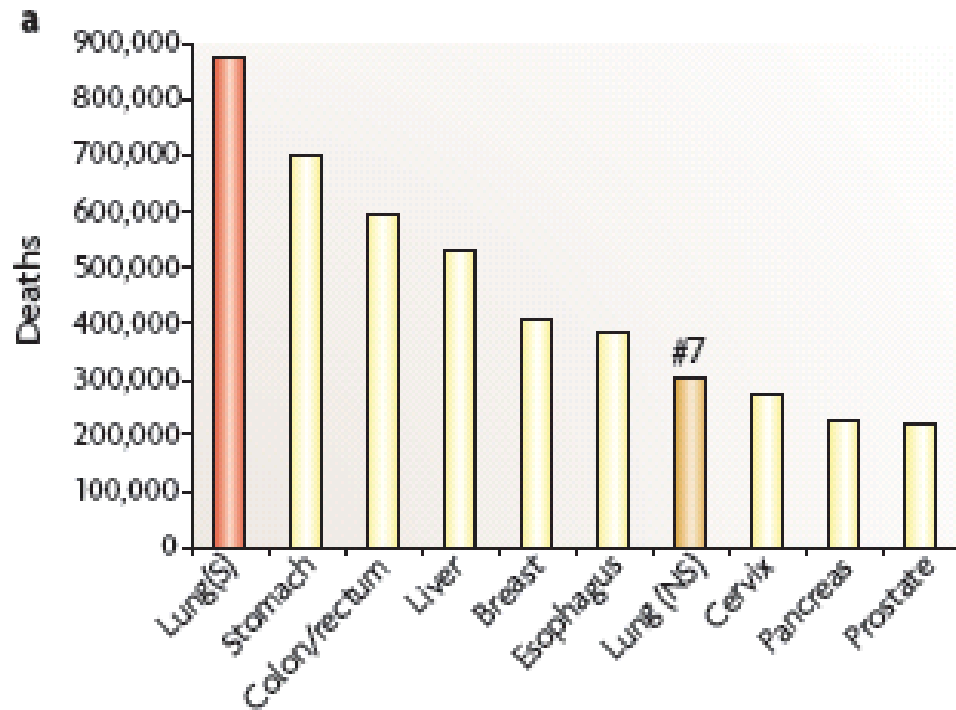


Overview

- Epidemiology
- Screening
- Diagnosis
- Staging
- Treatment
- Cases



Epidemiology



- Leading cause of cancer death in men and women worldwide
- 25% never smokers
- Prognosis is poor



Risk Factors

- Causal relationship between smoking and lung cancer well established
- Other risk factors: environmental tobacco smoke, radon, arsenic, air pollution, asbestos, silica, cooking fumes, and family history



Screening

- 75% of patients with lung cancer are incurable at diagnosis
- Prevention is the most effective strategy to reduce burden in the long term
- Potential benefit of screening to detect early cancers that can be cured



Screening

- National Lung Screening Trial (NLST): low dose CT (LDCT) vs. chest x-ray screening in high risk group (current or ex-smokers age 55 to 74; at least 30 pack-years)
- 20% reduction in lung cancer mortality with LDCT screening



Screening

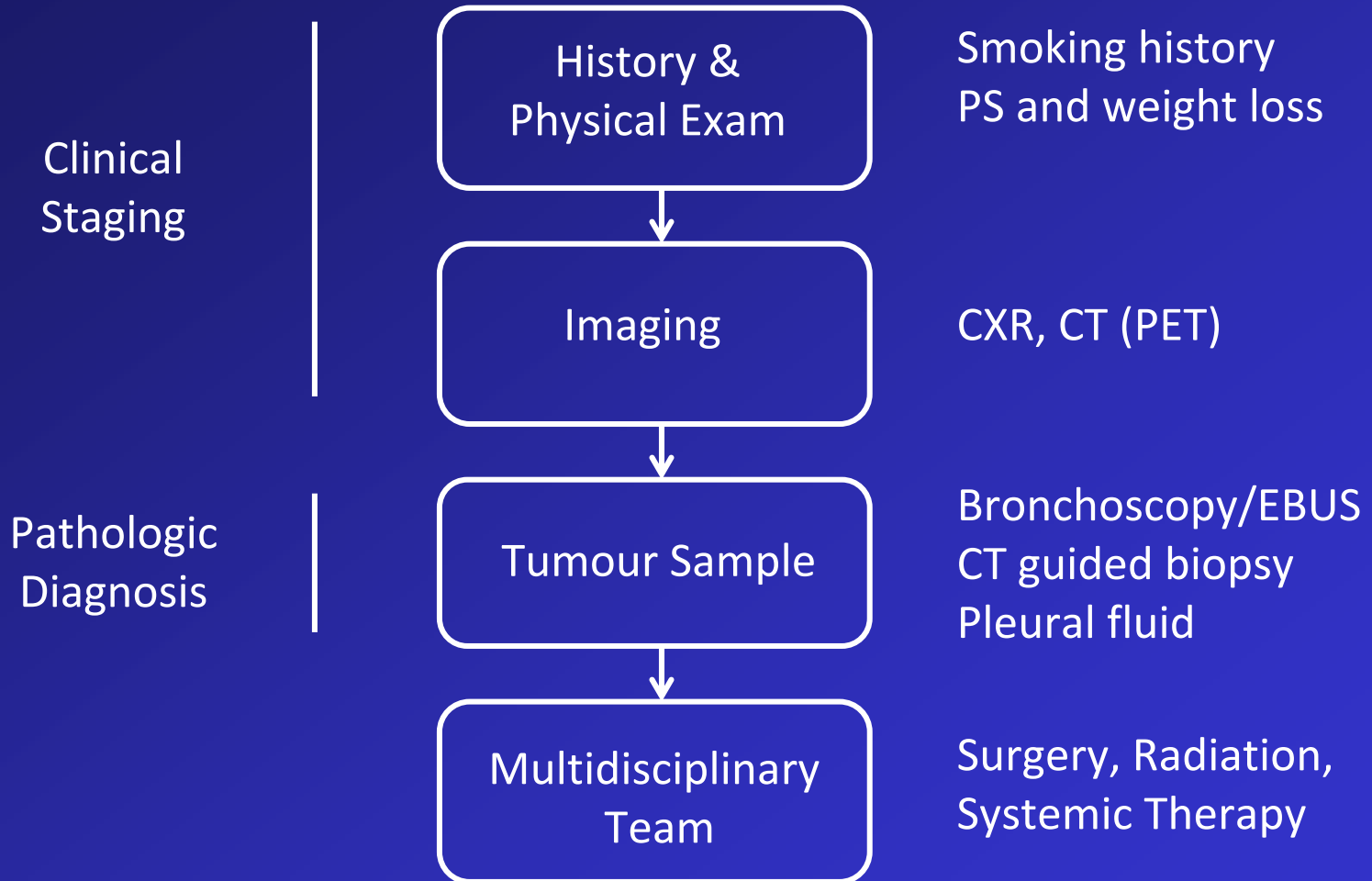
- Generalizability of NLST findings uncertain:
 - demographic of trial patients
 - expertise of academic centres
 - cost effectiveness
 - risk of false-positive findings
- Multiple studies ongoing to confirm NLST findings and screening pilot programs in development



Diagnosis and Staging



Suspected Lung Cancer



Clinical Staging

- To evaluate extent of disease involvement and identify targetable lesion for biopsy



Clinical Staging

- History and Physical
- CXR
- CBC, lytes, Cr, LFTs, Ca, alb, INR/PTT, CEA
- CT chest
- PET scan if:
 - Potentially curative treatment (stage I, II or III)
 - For staging prior to resection of solitary brain met
 - For radiation planning



Tissue Diagnosis

- Goal is to obtain adequate tissue to confirm diagnosis and perform molecular testing if indicated
- Ideally should target biopsy that will yield most advanced site of disease



Tissue Diagnosis

- Often difficult to obtain adequate tissue
- Surgical resection > Core biopsy > Bronchoscopy or EBUS > FNA or Fluid cytology



EBUS



- Relatively new procedure for tissue diagnosis and lymph node staging
- Can perform trans-bronchial needle aspirates (TBNAs) to obtain tissue from lungs and lymph nodes
- Allows for improved visualization for difficult to reach areas and to access small lymph nodes

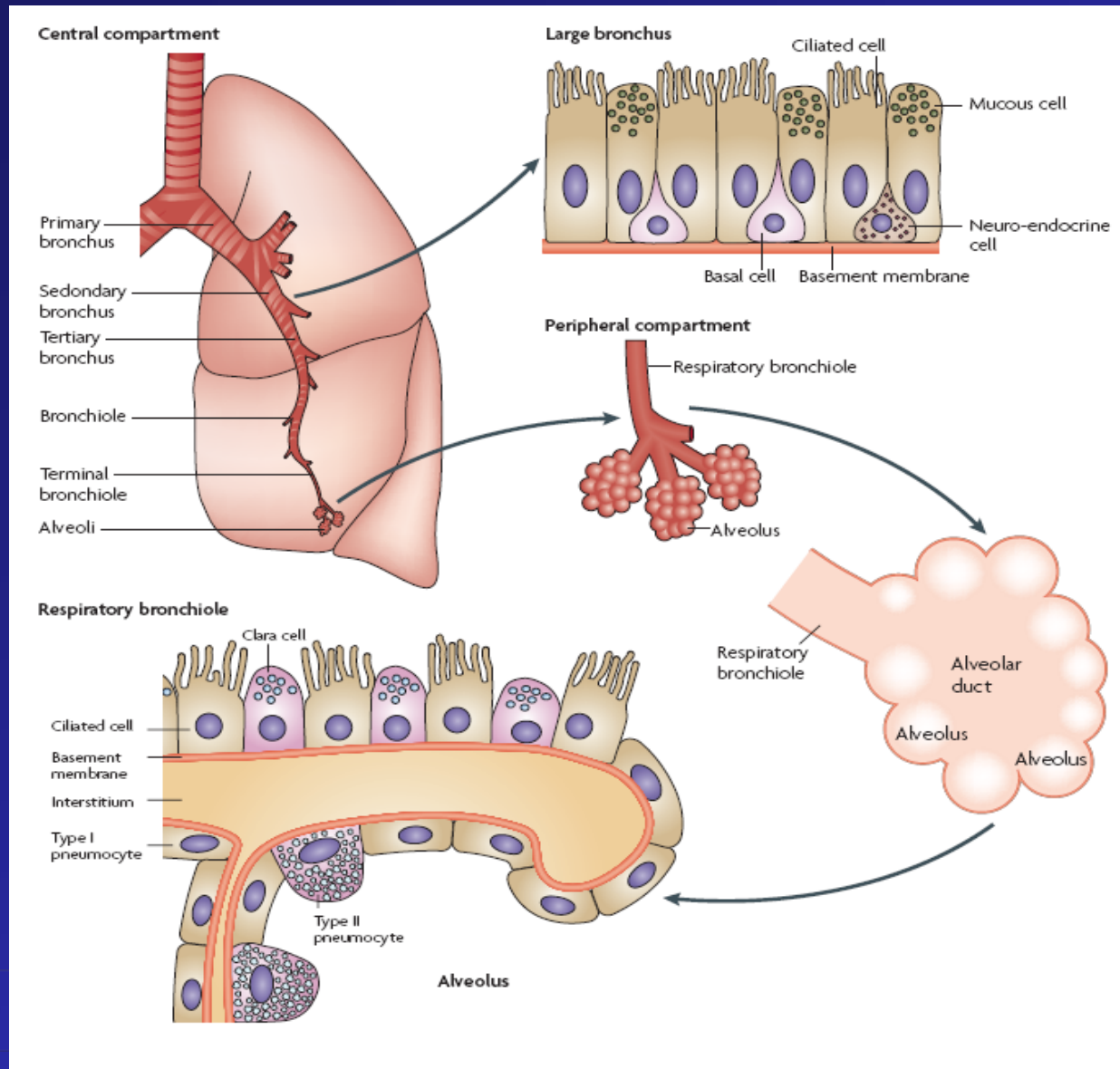


Tissue Diagnosis

- Non-small cell lung cancer (NSCLC) – 85%
 - Adenocarcinoma (ADC)
 - Squamous cell (SCC)
 - Large cell (LC)
- Small cell lung cancer (SCLC) – 10-15%



Clinical Features and Histology



Central
SCLC, SCC

Peripheral
ADC



Treatment



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General Principles

- Treatment is based on multiple factors
 - Stage
 - Histologic subtype
 - Tumour location
 - Age, comorbidities, performance status, weight loss



General Principles

- Identify goals of care: Palliative vs Curative
- Local Therapy: Surgery, Radiation
- Systemic Therapy: Chemotherapy, Targeted Rx
- Supportive Care: PleurX, opioids, home care, advanced care planning



NSCLC: Treatment and Outcomes

Stage	Treatment	5 yr survival
I	Surgery +/- Chemo	50%
II (IIIA)	Surgery +/- Chemo	40%
IIIA	ChemoRT +/- Surgery	20-30%
IIIB	ChemoRT or RT alone	5-10%
IV	Chemo +/- Targeted Therapies	1%

NSCLC: Targeted Therapies

- Recent discovery of subsets of NSCLC with mutations that drive cancer growth and spread
- These lung cancers are highly responsive to treatments that target these mutations
- More frequent in never smokers
- Metastatic non-squamous NSCLCs are routinely tested for EGFR and ALK



SCLC: Treatment and Outcomes

Stage	Treatment	5 yr survival
Limited	ChemoRT + PCI	10-20%
Extensive	Chemo +/- RT	1-2%



Cases

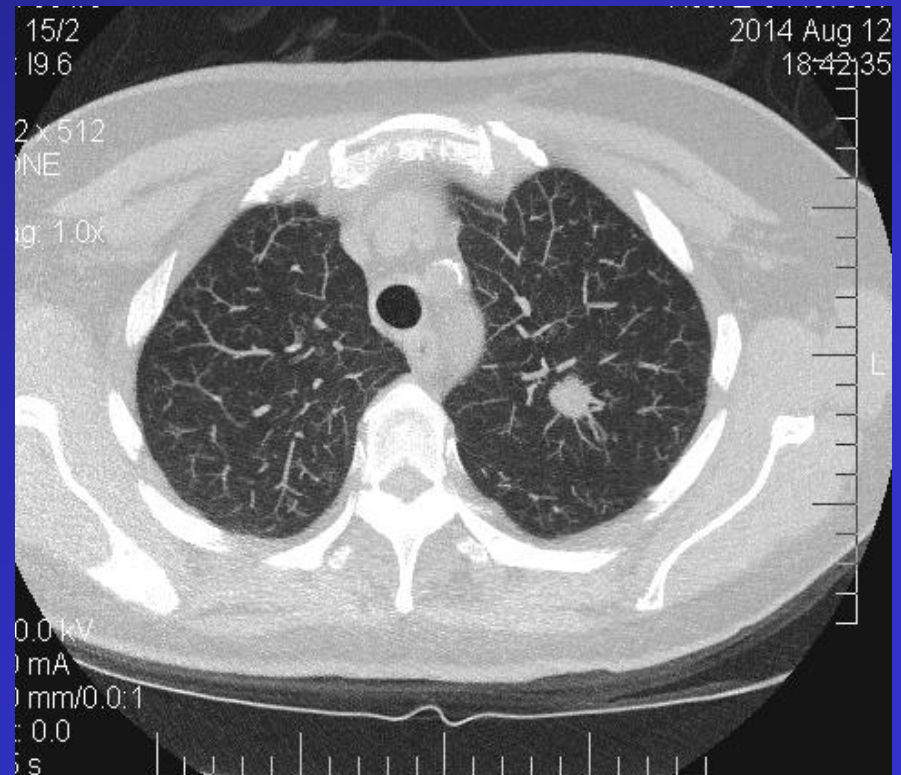
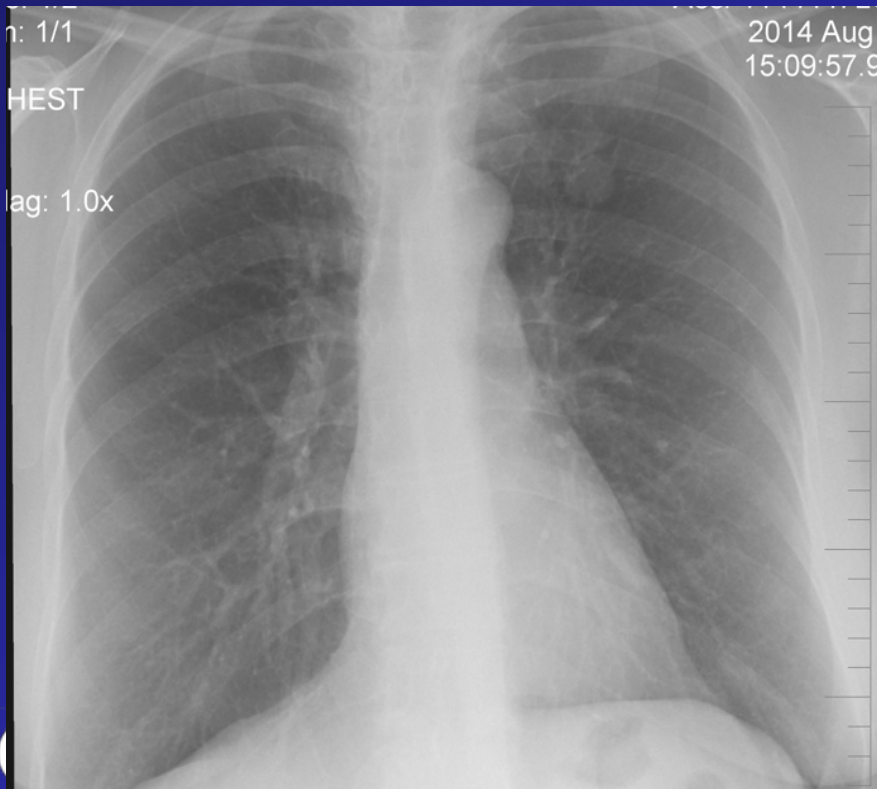
- Adjuvant NSCLC
- Locally Advanced NSCLC
- Metastatic NSCLC



Case 1

58 year old woman, smoker

- Presents with atypical chest pain Aug 2014



Case 1

- Referred to Respiriology
- Bronchoscopy Aug 29 2014 – non-diagnostic
- EBUS Sep 8 2014 – non-diagnostic
- EBUS Sep 24 2014 – atypical cells
- What next?



Case 1

- Consult Thoracic Surgery
- PET - no nodal or distant disease (cT1N0)
- LUL lobectomy Nov 2014
- Pathology
 - pT1a (1.7cm) poorly differentiated adenocarcinoma
 - pN2 (5 and 7L nodes positive)
 - Stage IIIA



Case 1

- 5-year survival without chemo 30%; with chemo 40%
- CT head negative
- Postoperative chemo: cisplatin/vinorelbine x 4
- Referred to ?Post-operative RT (N2 disease)



Case 1 Key Points

- ~30% of patients are diagnosed with operable disease
- Tissue diagnosis can be difficult and consider referring to avoid delays and repeat procedures
- Surgical resection for tissue diagnosis and treatment may be required



Case 1 Key Points

- For operable disease, PET and pathologic nodal staging (EBUS) required
- Clinical (pre-op) and pathologic (post-op) stage can differ
- Adjuvant chemotherapy provides modest benefit in resected stage I-III NSCLC
- Post-operative RT for resected N2 disease is controversial



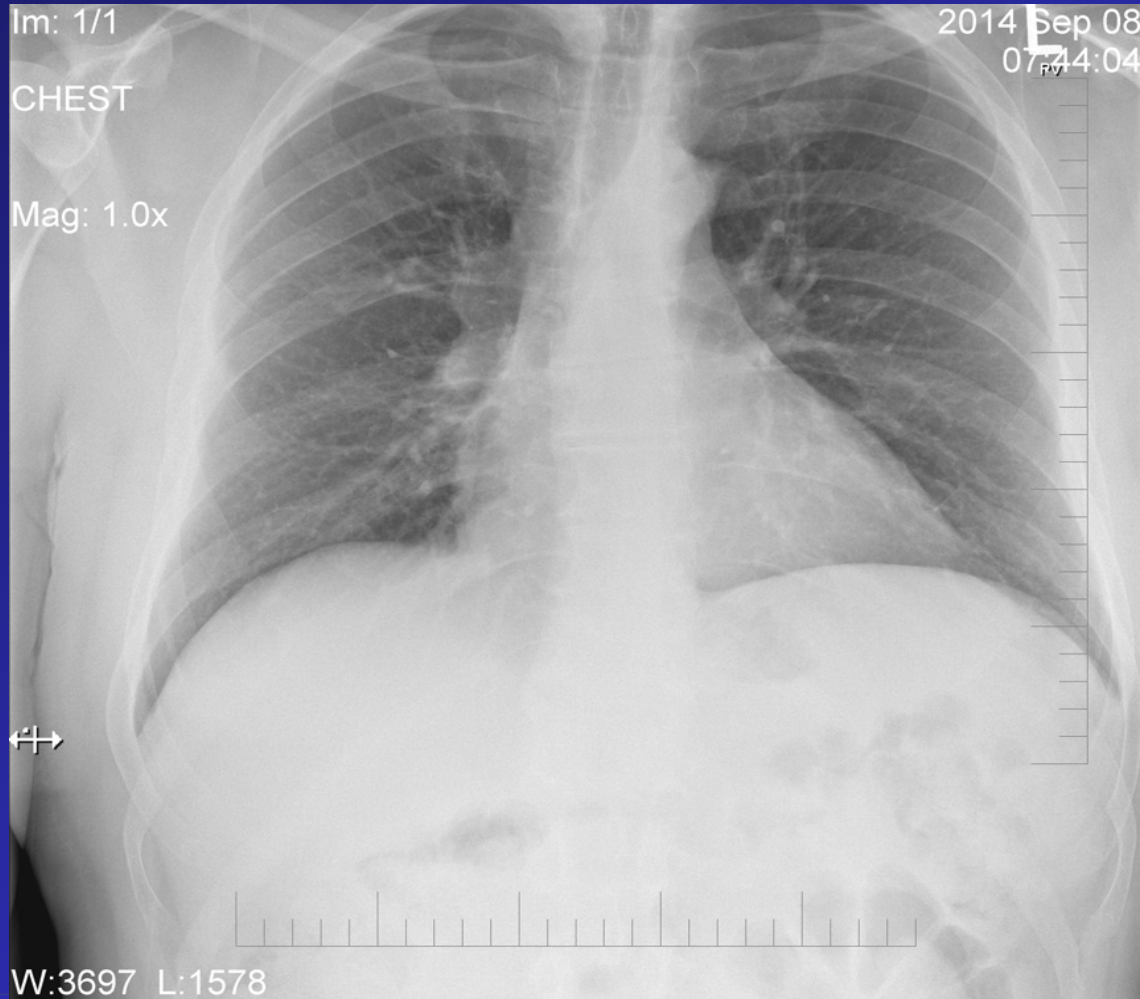
Case 2

48 year old man, 30 pack-year ex-smoker

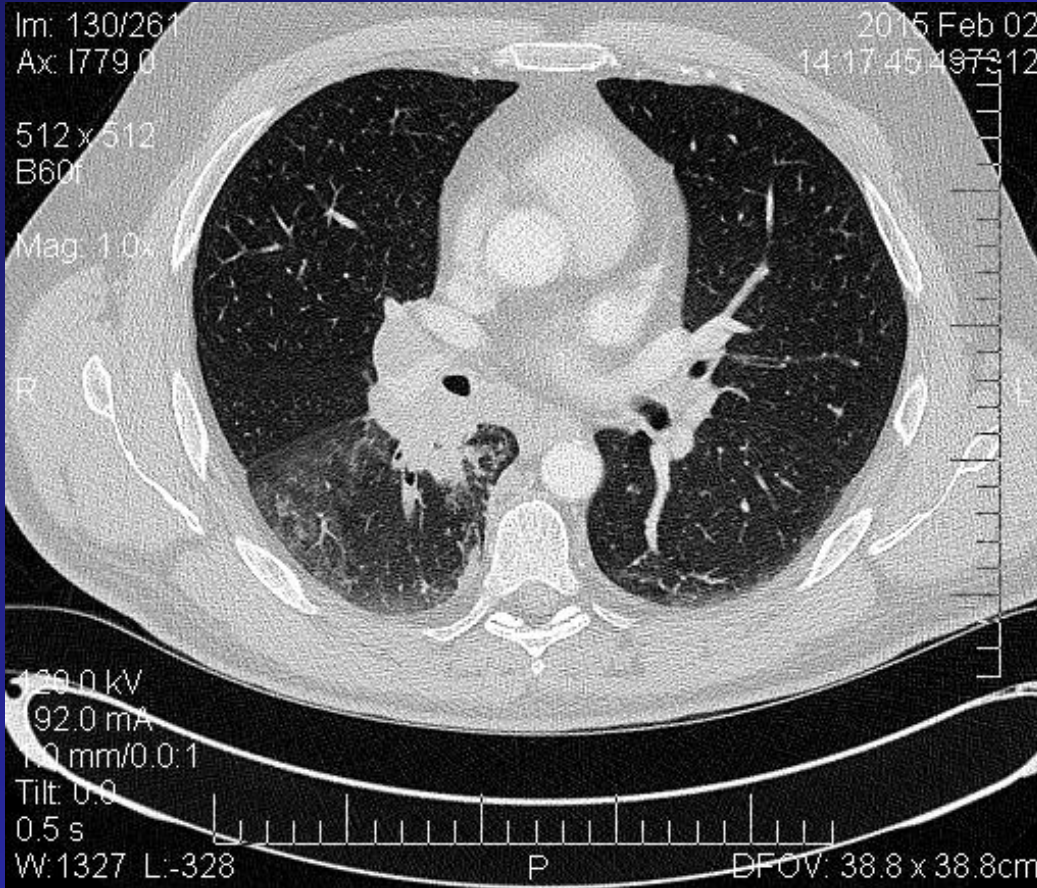
- Cough June 2014
- Treated as GERD with PPI
- Heartburn better, but persistent cough



CXR



Case 2



- PFTs Nov 2014 normal
- Referred to Respiriology Jan 2015

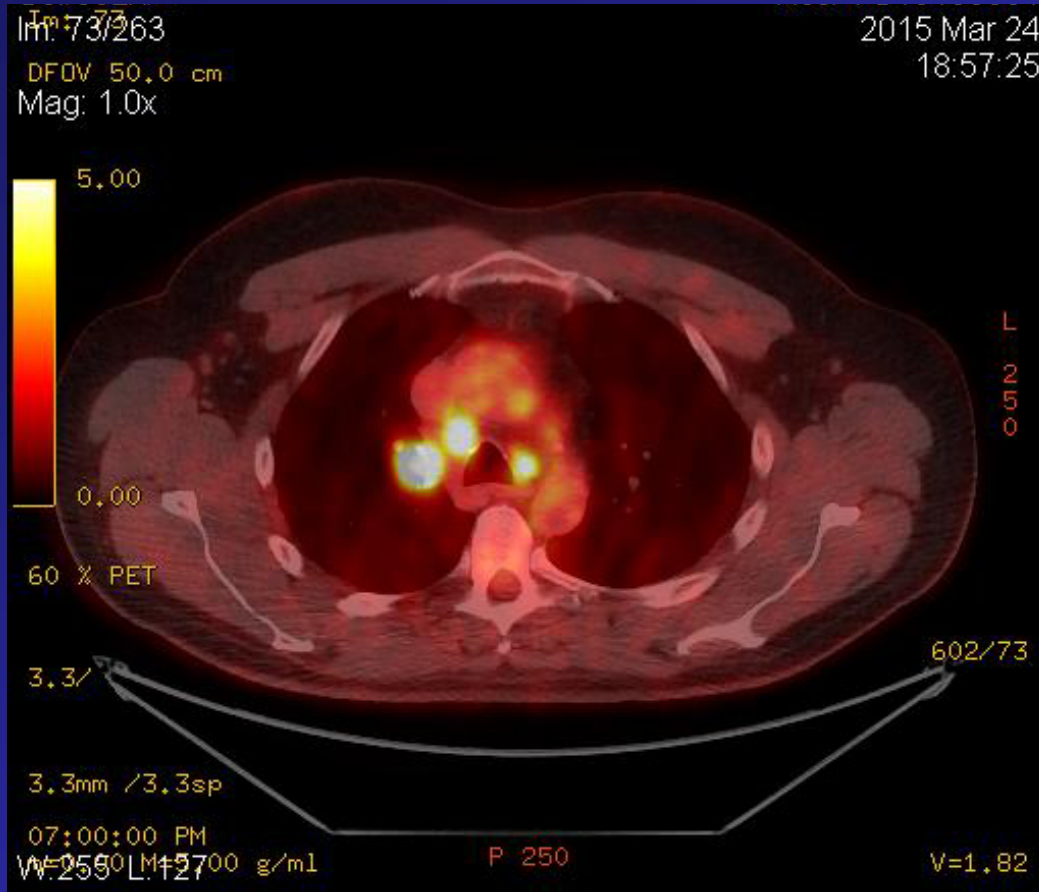


Case 2

- Bronchoscopy Feb 2015 VGH: non-diagnostic
- EBUS Feb 2015 VGH:
 - Squamous cell ca RLL
 - Station 4R, 7, 11R nodes +
 - 4L node non-diagnostic



Case 2



- R neck and bilateral mediastinal nodal involvement
- CT head negative
- Clinical stage IIIB (T2N3)

Case 2

- Concurrent chemoRT Apr 2015
- Cisplatin/Etoposide x 2 cycles during RT (60Gy; 6 weeks)
- Plan is to complete further 2 cycles of chemo after RT
- Goals of treatment are curative, but recurrence rate is very high ~90%



Case 2 Key Points

- CXR as a screening and diagnostic tool can be limited
- Consider CT and/or Respiriology consult with persistent cough if high risk
- Delays from symptom onset to diagnosis and treatment common
- Multiple bottle-necks = need for multidisciplinary rapid access clinic



Case 2 Key Points

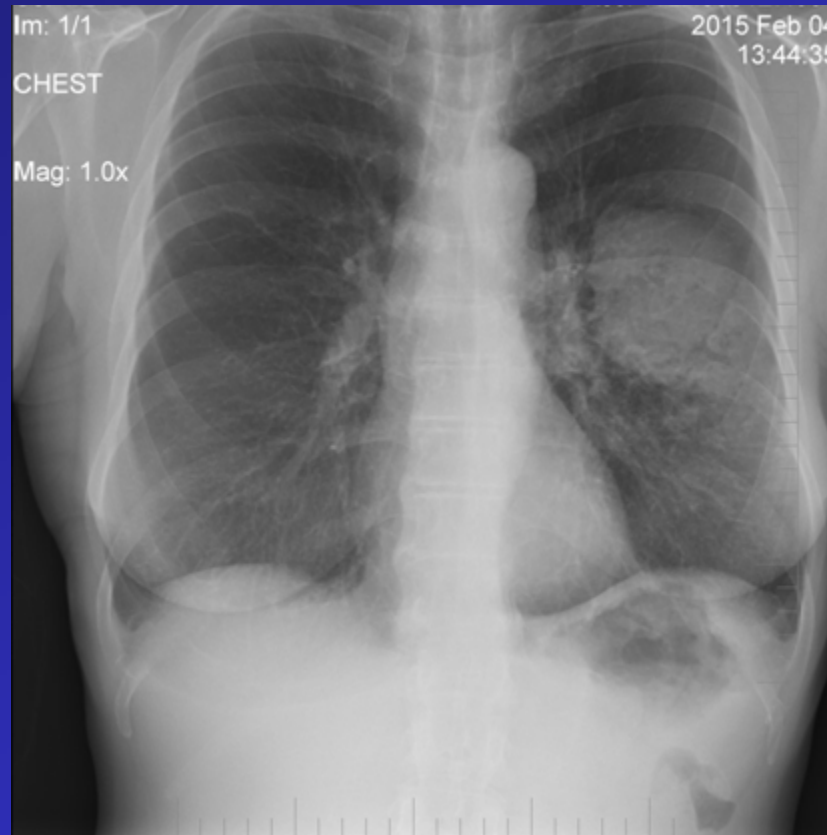
- Concurrent chemoRT is an option for fit patients with locally advanced disease that is amenable to high dose RT (60Gy)
- Stage IIIA NSCLC 5-year OS is 20% with concurrent chemoRT
- Stage IIIB NSCLC 5-year OS is 5-10%



Case 3

56 year old woman, smoker

Presents with cough and scant hemoptysis



Case 3

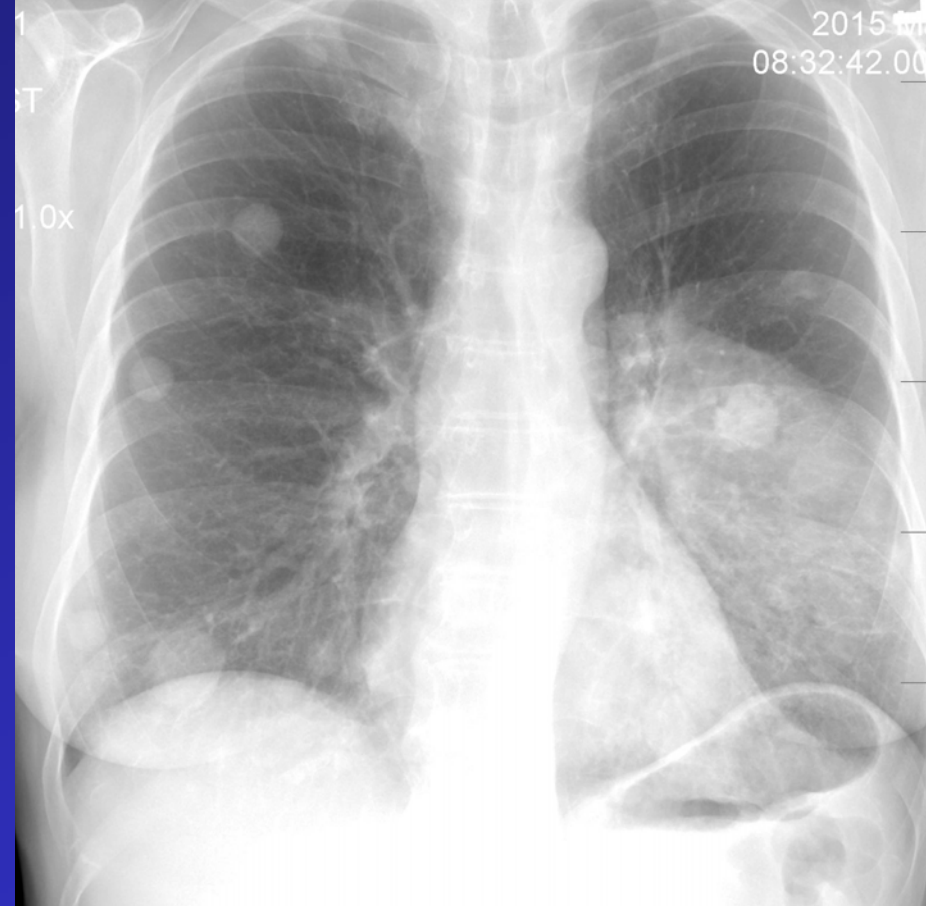
- CT Feb 2015: LUL mass, left hilar, mediastinal, adrenal and liver involvement
- EBUS Mar 2015 –NSCLC (adenoca)
- PET and CT head – brain and bone mets
- Palliative RT to lung and brain Mar 2015
- Molecular testing: EGFR/ALK negative
- Cisplatin/pemetrexed chemo x 1 cycle April 2015



Case 3



Pre-chemo



Post cycle 1



Case 3

- Switched to 2nd-line docetaxel
- Rapid clinical deterioration
- Transition to best supportive care



Case 3 Key Points

- Median survival of met NSCLC is 6 months without treatment
- First-line platinum-based chemotherapy prolongs survival by 3-6 months
- Response rates to 1st-line chemotherapy 30-50%
- Rapidly progressive disease on 1st-line chemotherapy = poor prognosis



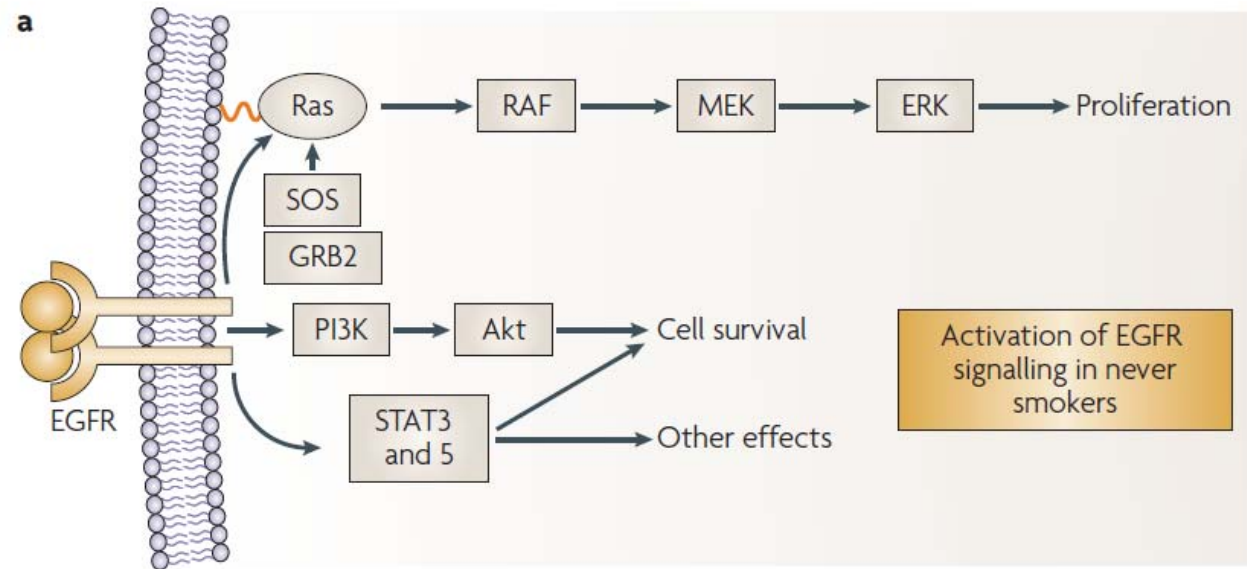
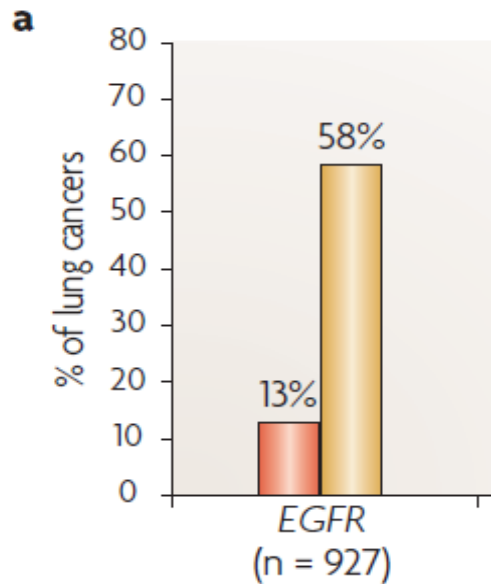
Case 4

88 year old Asian female lifelong never smoker

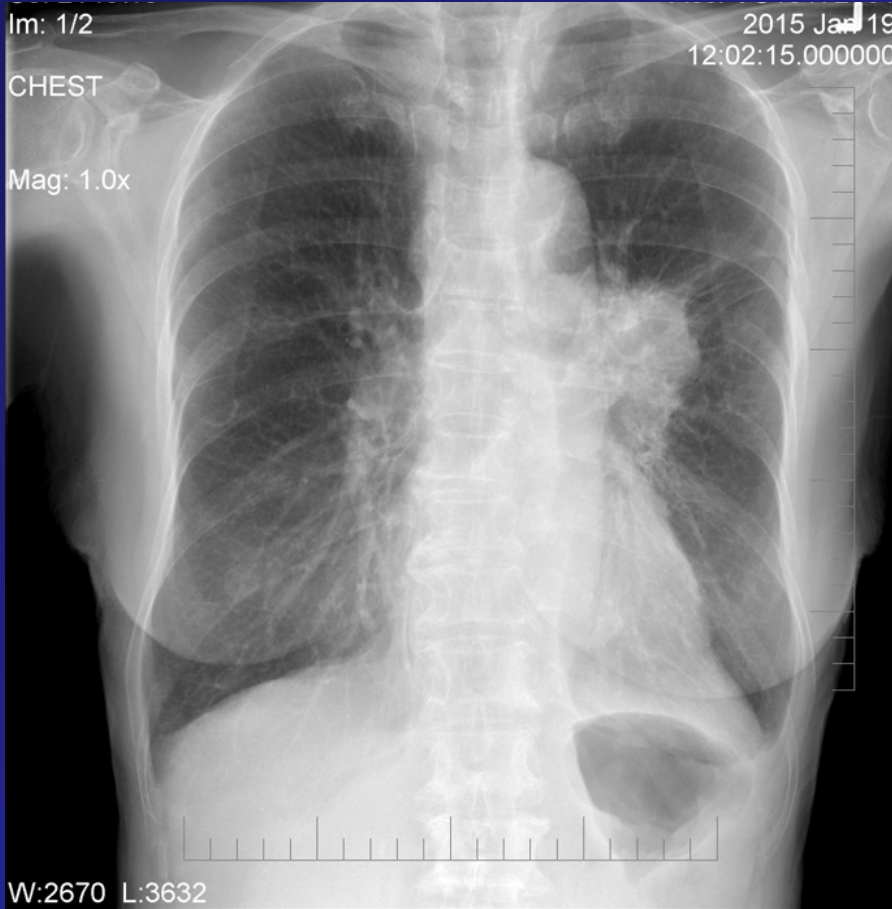
- Chest pain Oct 2014
- Dec 2014 CT: LUL mass, bilateral lung nodules, extensive bone metastases
- Family History: brother lung cancer age 81; sister lung cancer at age 63; sister uterine cancer age 31
- No known exposures
- Biopsy: NSCLC (adenoca); **EGFR mutation positive (L858R)**



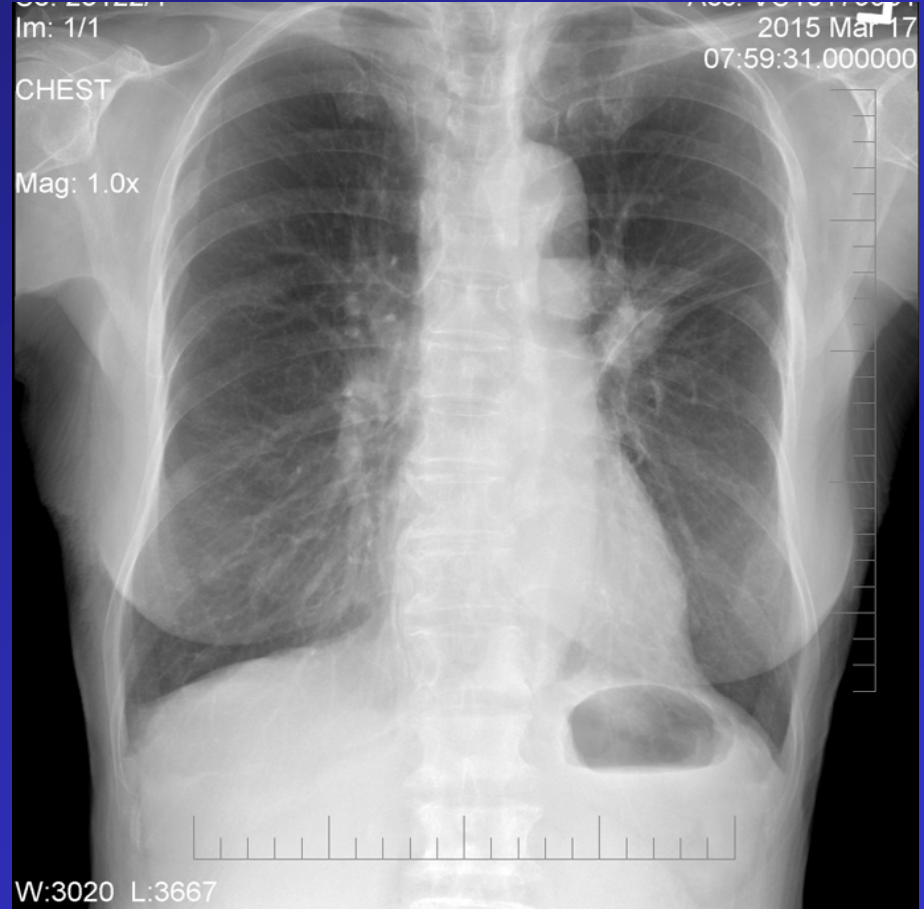
EGFR mutations in Lung Cancer



Case 1



Baseline



8 weeks post gefitinib

Case 4 Key Points

- Activating EGFR mutations are present in 15% of NSCLC in North America; 60% in Asian never smokers
- Presence of EGFR mutation predicts response to EGFR inhibitor therapy (gefitinib, erlotinib)
- Resistance ultimately develops
- Early results from clinical trials of newer generation EGFR inhibitors promising



Case 5

32 year old female never smoker

Presents with blurring of vision left eye and intermittent cough

Ophthalmology: metastatic lesions to left eye



Case 5



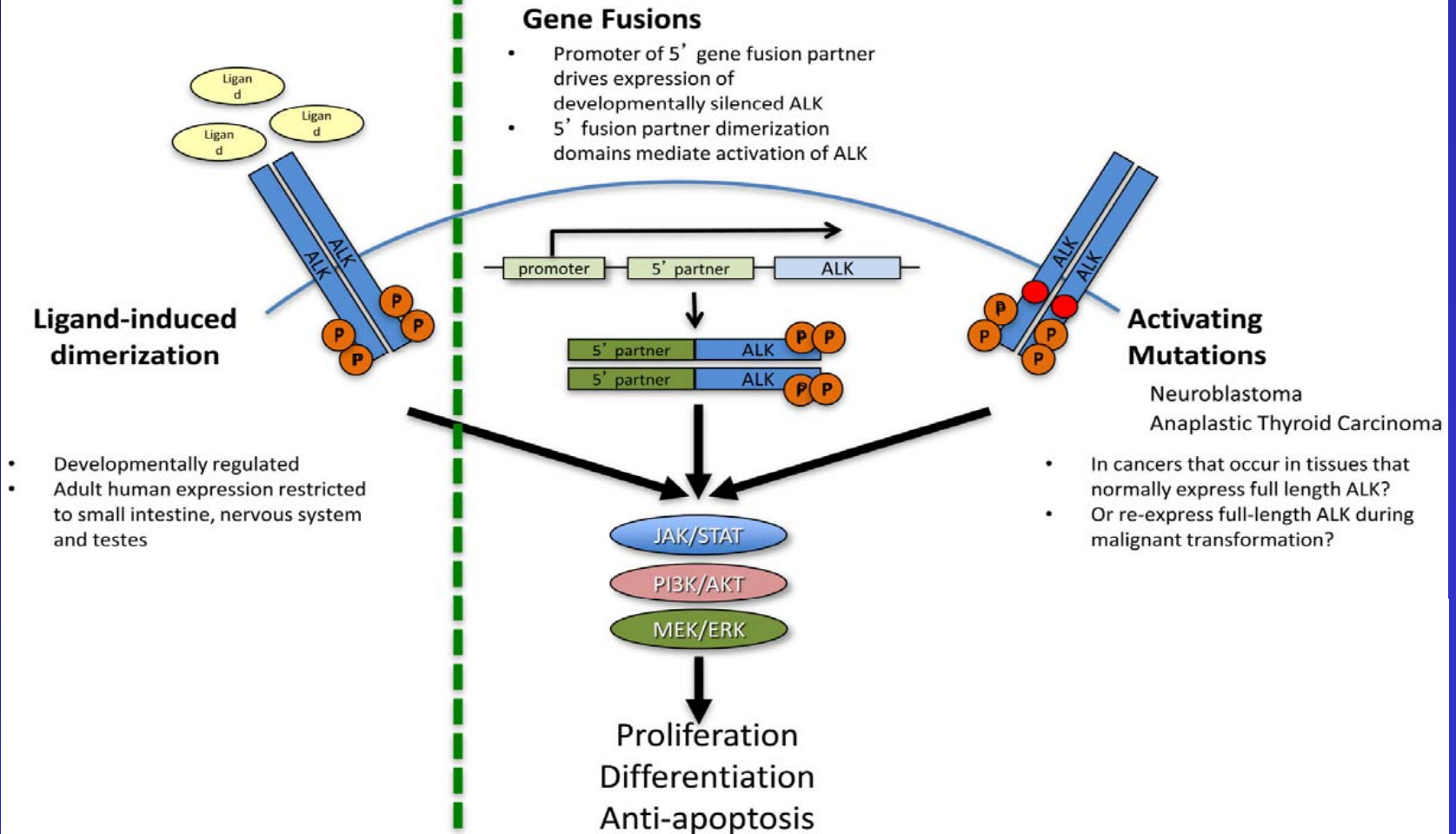
- CT showing collapse of L lung, brain, eye, and liver mets
- Core biopsy liver: adenoca consistent with lung primary
- ALK testing (IHC and FISH) positive



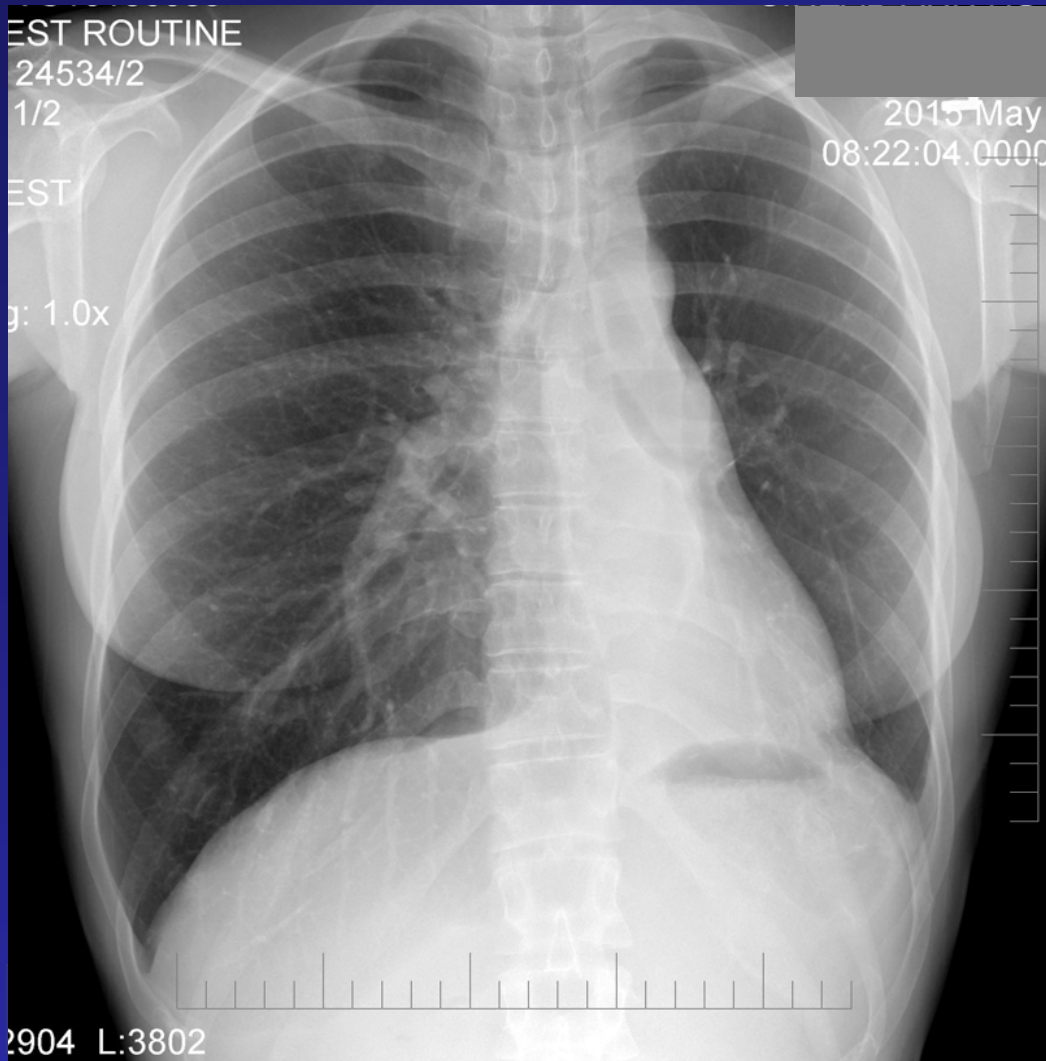
ALK

Normal ALK activation

Oncogenic ALK activation



Case 5



- Started on crizotinib
- Elected to hold off on RT to brain and eye
- CXR 4 weeks on crizotinib
- Eye lesion improving



Case 5 Key Points

- ALK-positive NSCLCs are highly responsive to ALK inhibitor therapy (crizotinib)
- CNS response to crizotinib have been observed
- However, resistance ultimately develops
- Clinical trials with newer generation ALK inhibitors are underway



Metastatic NSCLC

	Non-squamous		Squamous	
	EGFR+	ALK+	EGFR/ALK-	N/A
1 st -line	Gefitinib/Erlotinib	Crizotinib	Platinum doublet	Platinum doublet
2 nd -line	Platinum doublet	Platinum doublet	Pemetrexed or Docetaxel	Docetaxel
3 rd -line	Pemetrexed or Docetaxel	Pemetrexed or Docetaxel	Erlotinib	Erlotinib



Summary Recent Advances

2005 to present...

- NLST and LDCT screening
- First PET scan at BCCA
- EBUS for nodal staging
- Minimally invasive surgeries
- Targeted radiation techniques (stereotactic RT) for inoperable stage I disease
- Approval of molecular testing and targeted therapies for EGFR+ and ALK+ metastatic NSCLC



Future Directions

2015 and beyond...

- Better understanding of risk factors for lung cancer in never smokers
- Guidelines for LDCT screening in high risk groups
- Improved techniques for rapid diagnosis and treatment (liquid biopsy)
- Towards personalized genomics and targeted therapies
- Ongoing studies of immunotherapy



Thank You



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