Cystic Lung Diseases

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HARVARD MEDICAL SCHOOL | Postgraduate Medical Education

Disclosure

No conflict of interest

Learning Objectives

- Identify causes of cystic lung diseases

- Awareness of linkage between cystic lung disease and genetic inheritable disorders

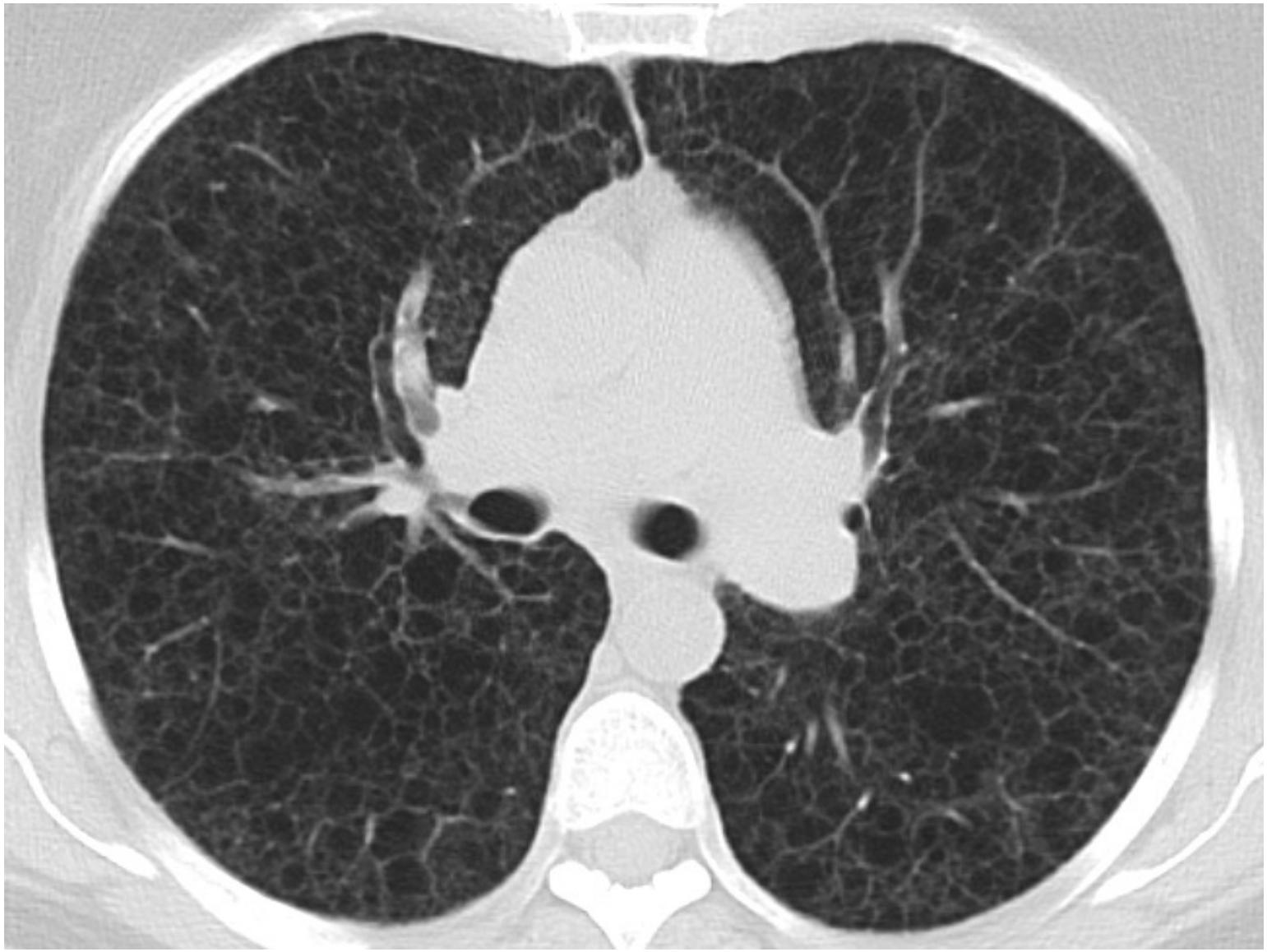
Cystic lung diseases

Centrilobular emphysema
Pulmonary metastasis
Subacute (?chronic) hypersensitivity pneumonitis
Desquamative interstitial pneumonia
Barotrauma/ ARDS
Pulmonary infection- pneumatoceles
Necrobiotic nodules
Light chain disease

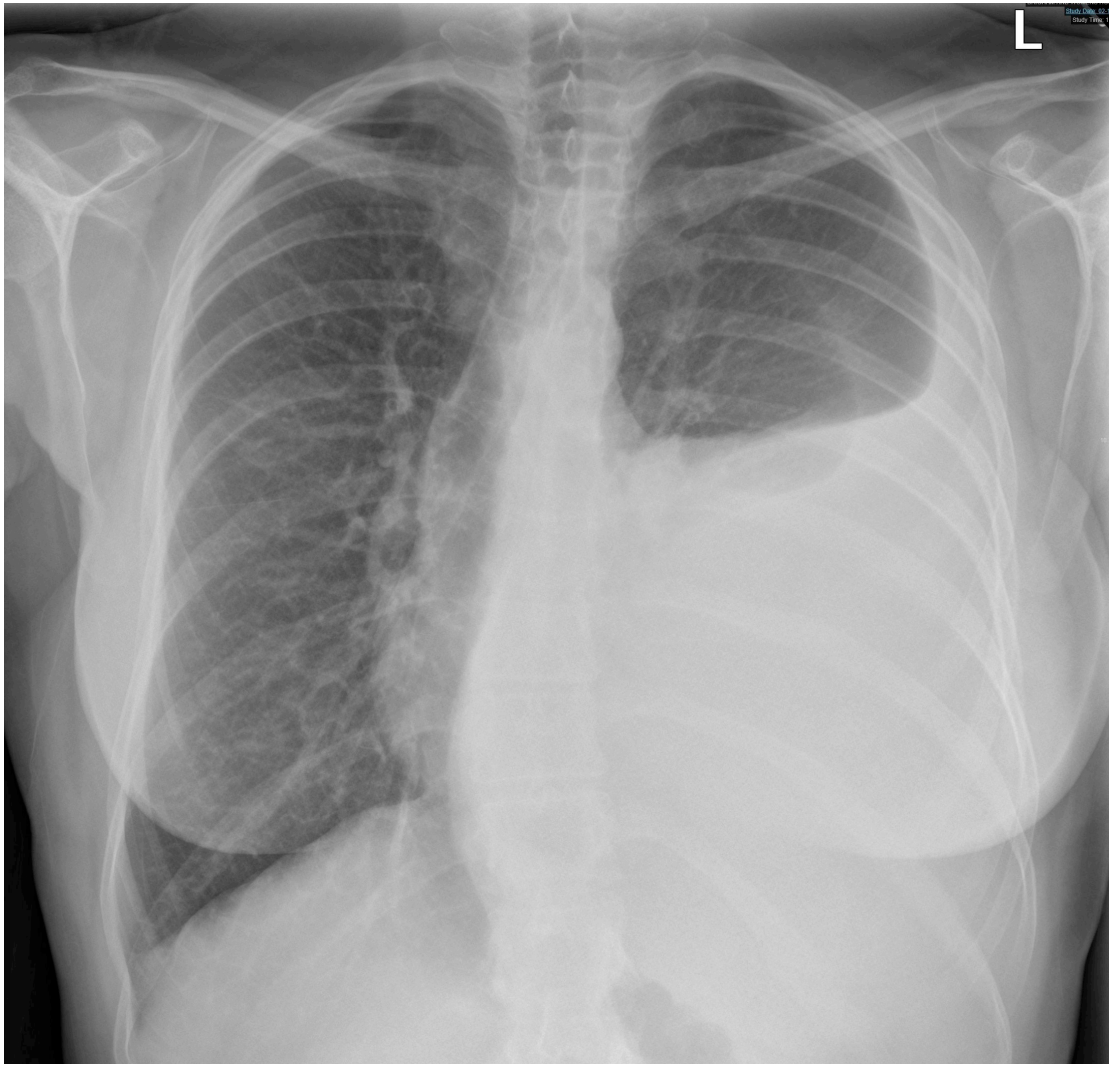
Lymphangioleiomyomatosis
Langerhans cell histiocytosis
Birt Hogg Dube syndrome
Lymphoid interstitial pneumonia

Beddy et al. Insights Imaging 2011 2:1-7

Cystic lung changes in LAM



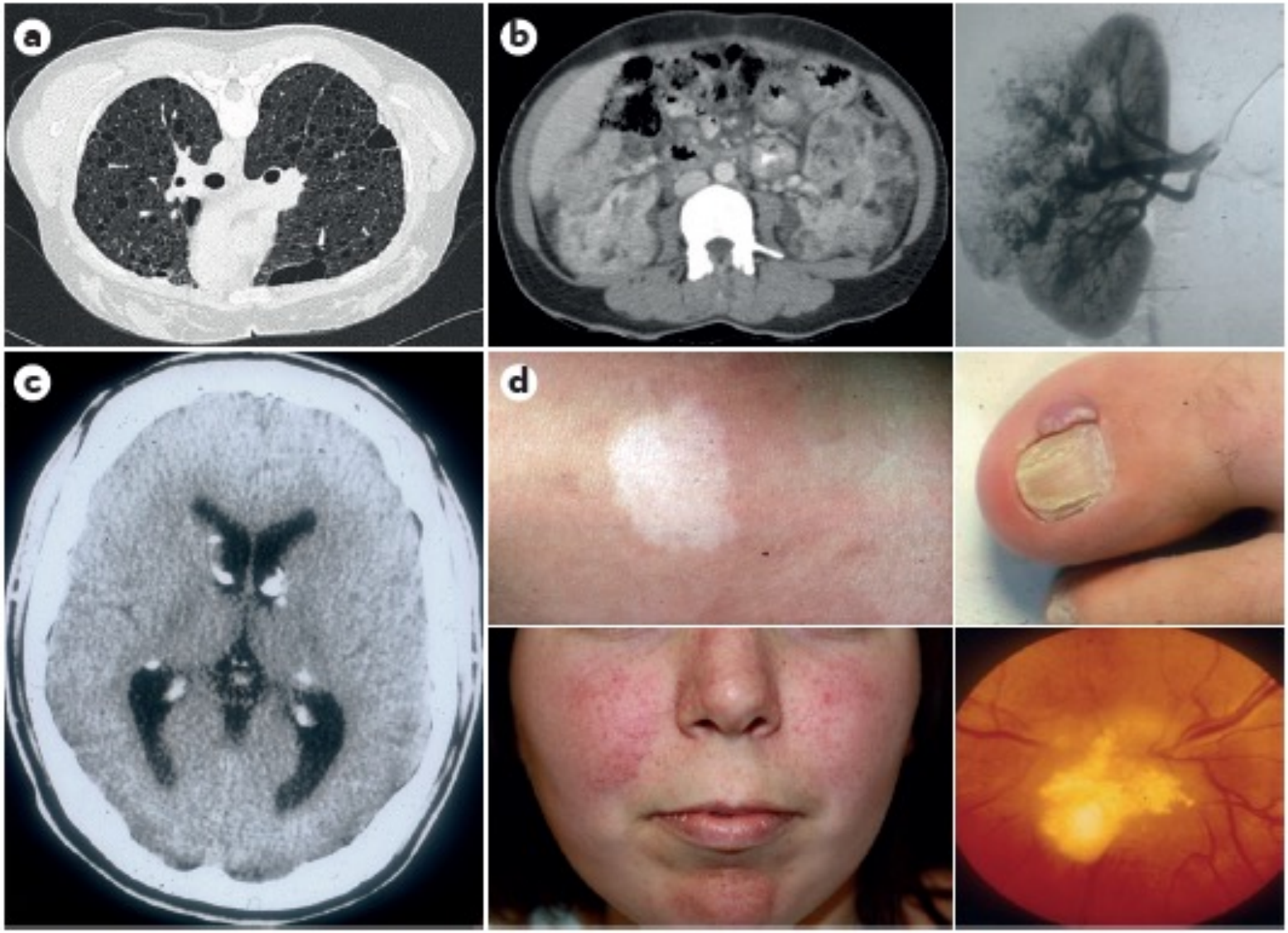
Chylous effusion



Screening for TSC

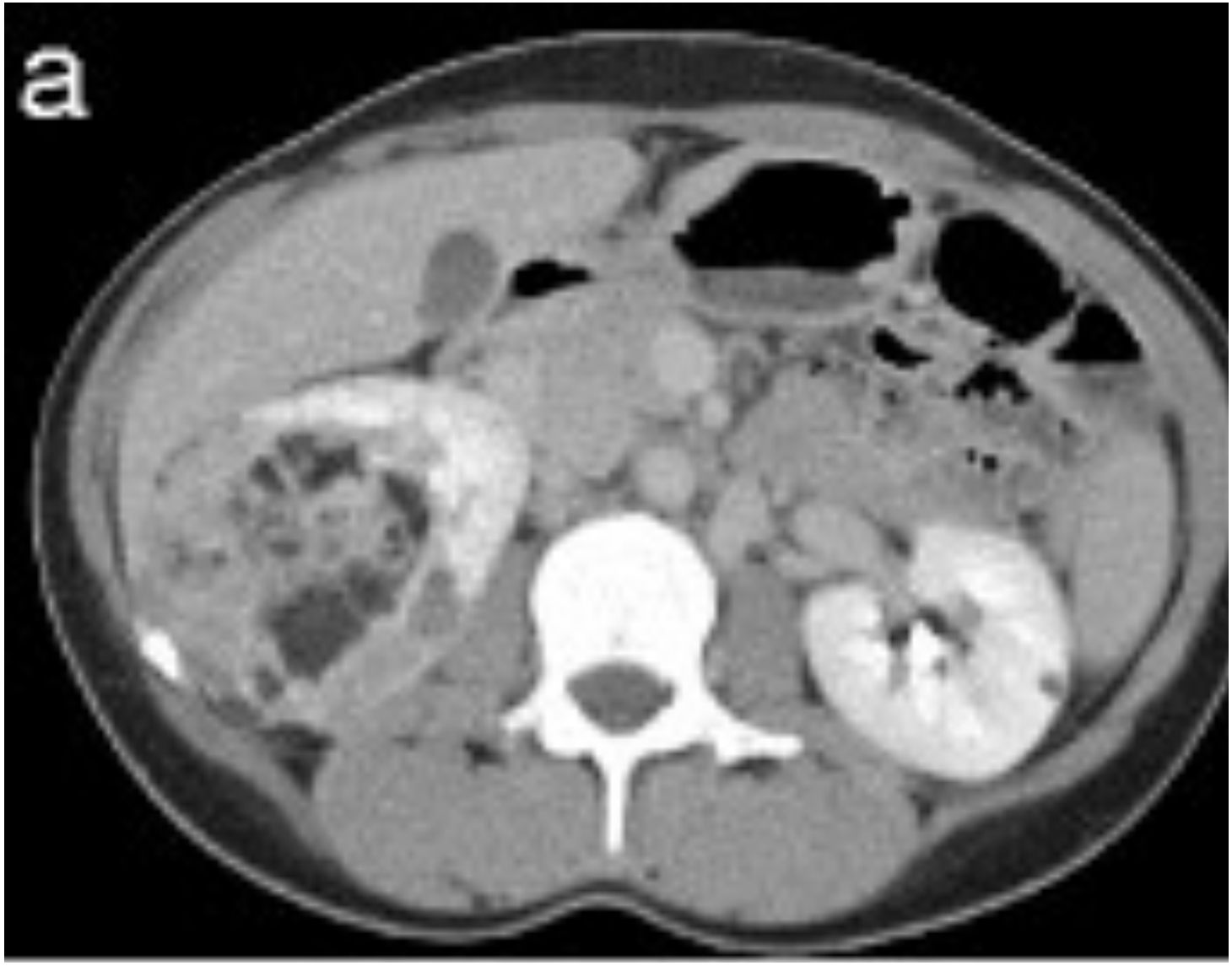
- Personal and family history
- Skin lesions
- Bilateral AML
- Brain lesions

Tuberous Sclerosis Complex



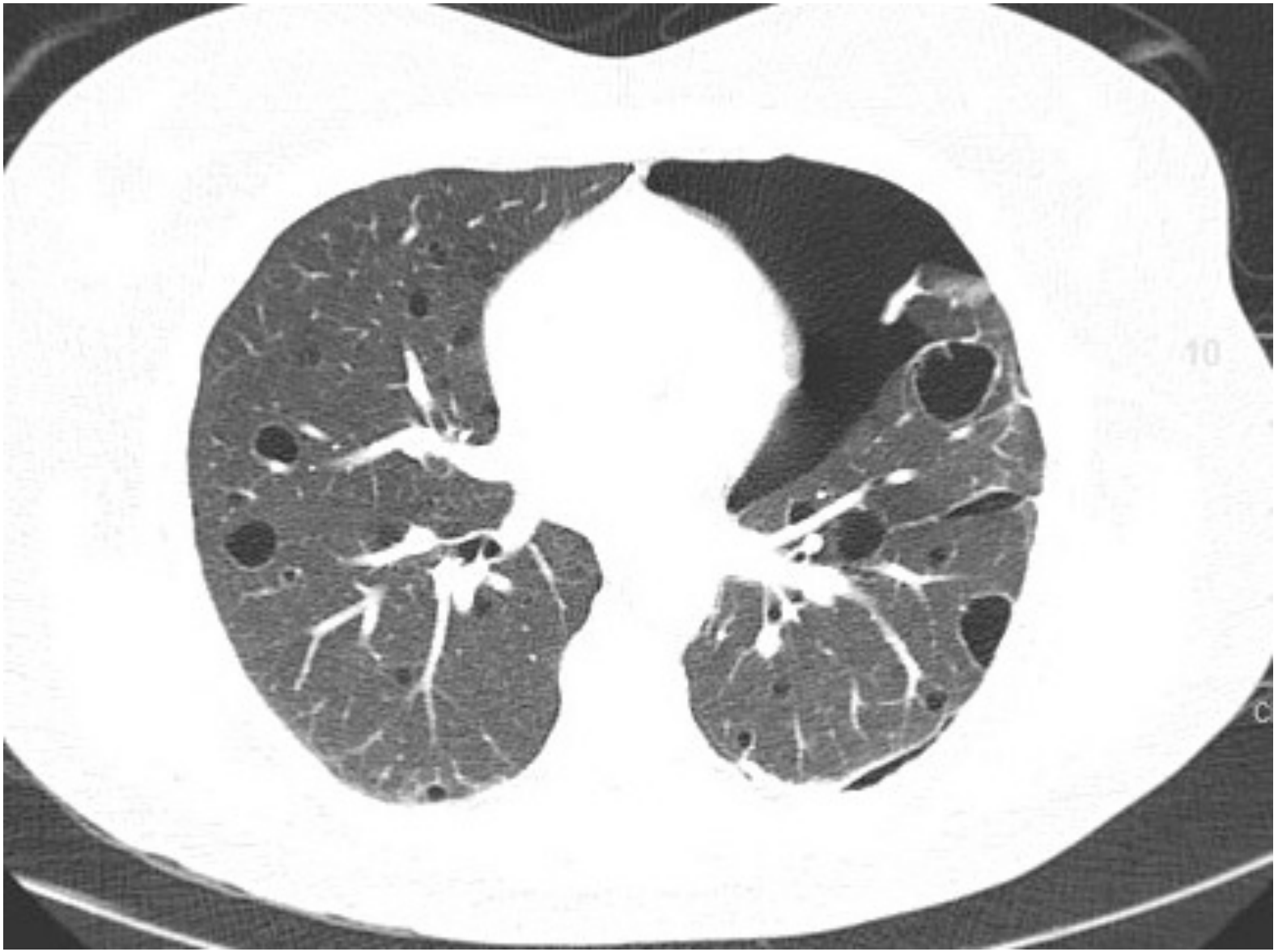
Henske et al. Nature Reviews 2016; Carsillo et al PNAS 2000

Angiomyolipoma (AML)



Yeoh et al. 2014 Orphanet Journal of Rare Diseases

Pneumothorax

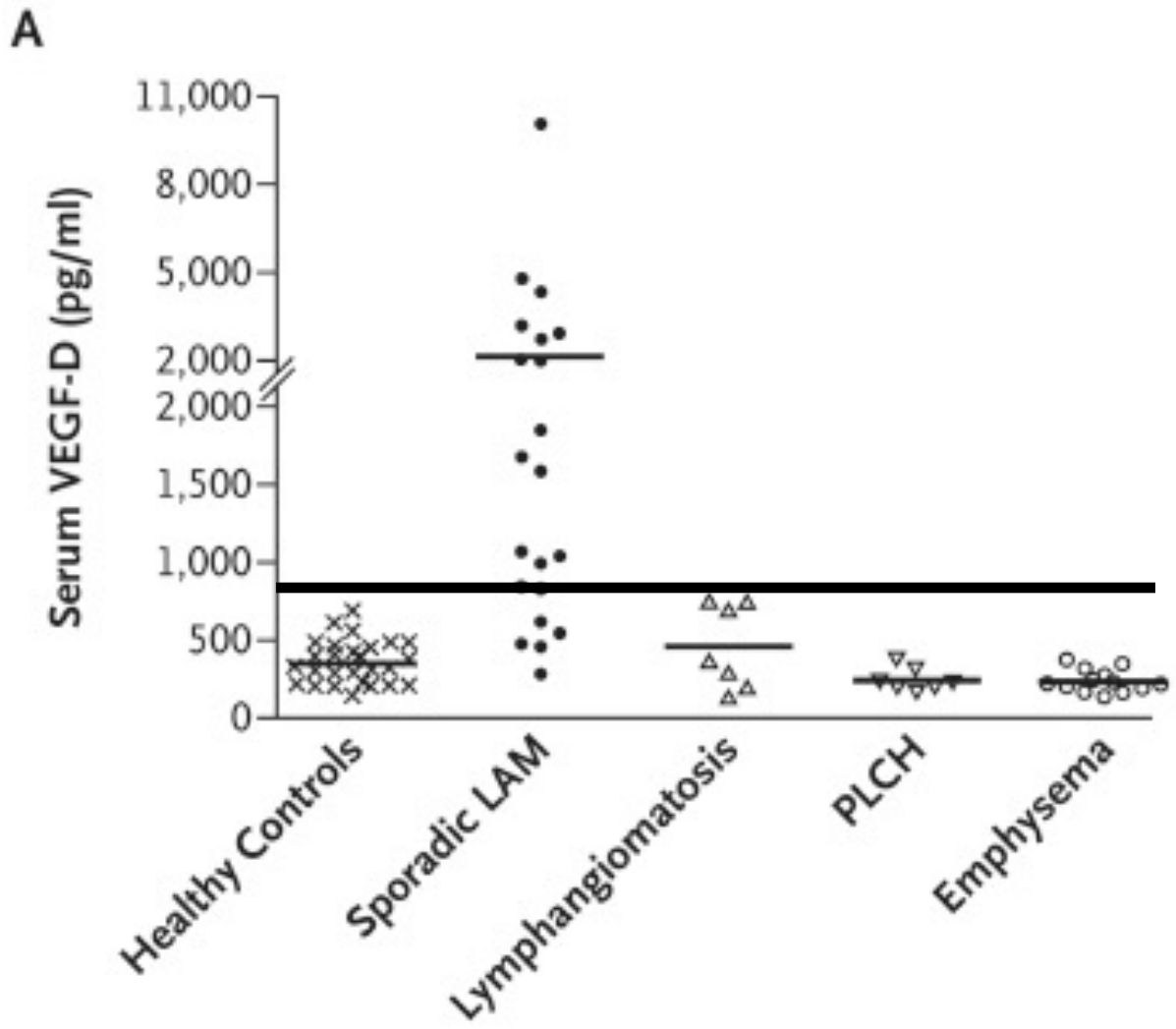


Pneumothorax

- 40% at the time of diagnosis
- 60% at some point
- Risk of recurrence high (>70%)

Johnson et al. ERJ (2010); Almoosa et al. Chest (2006)

VEGF-D a biomarker for LAM



Young et al. N Engl J Med (2008)

Diagnostic criteria of LAM

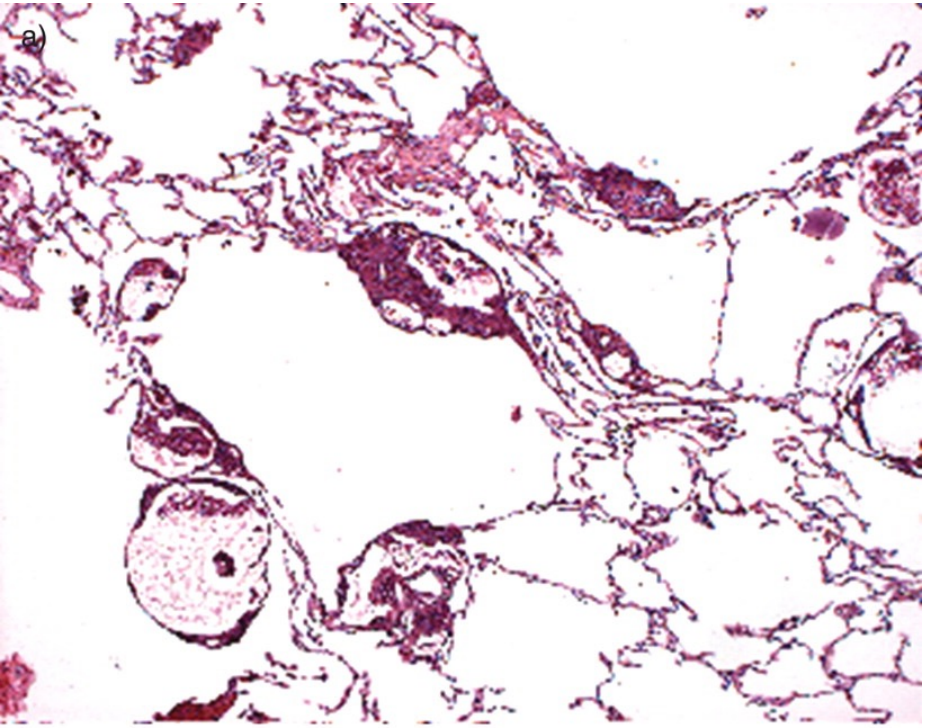
- Typical cystic changes

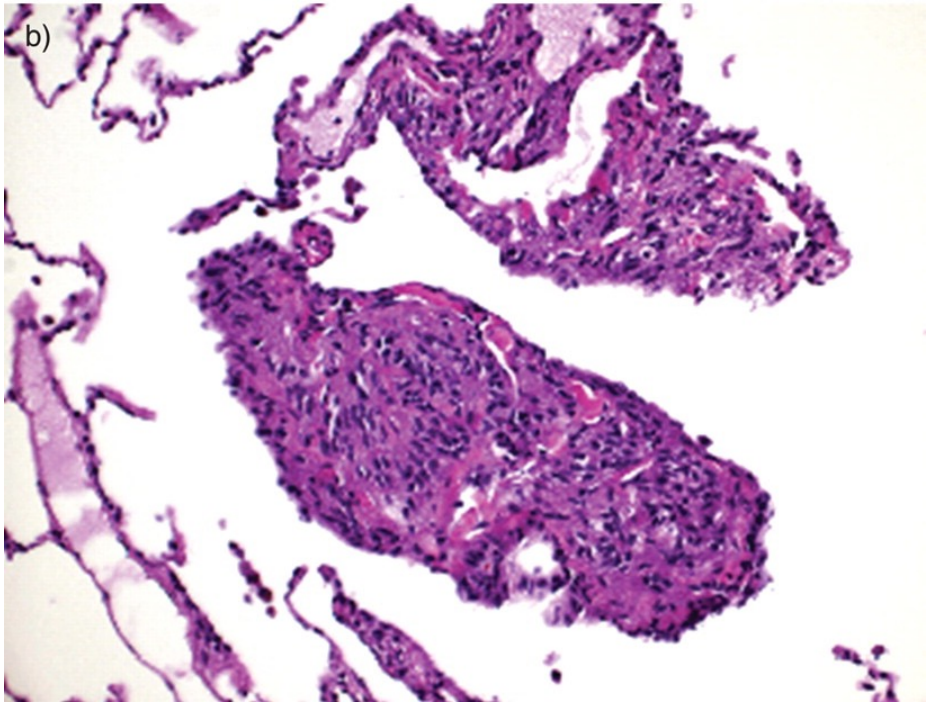
+ **any**

- AML
- Chylous effusion
- VEGF-D >800pg/ml

McCormack et al. Am J Respir Crit Care Med 2016

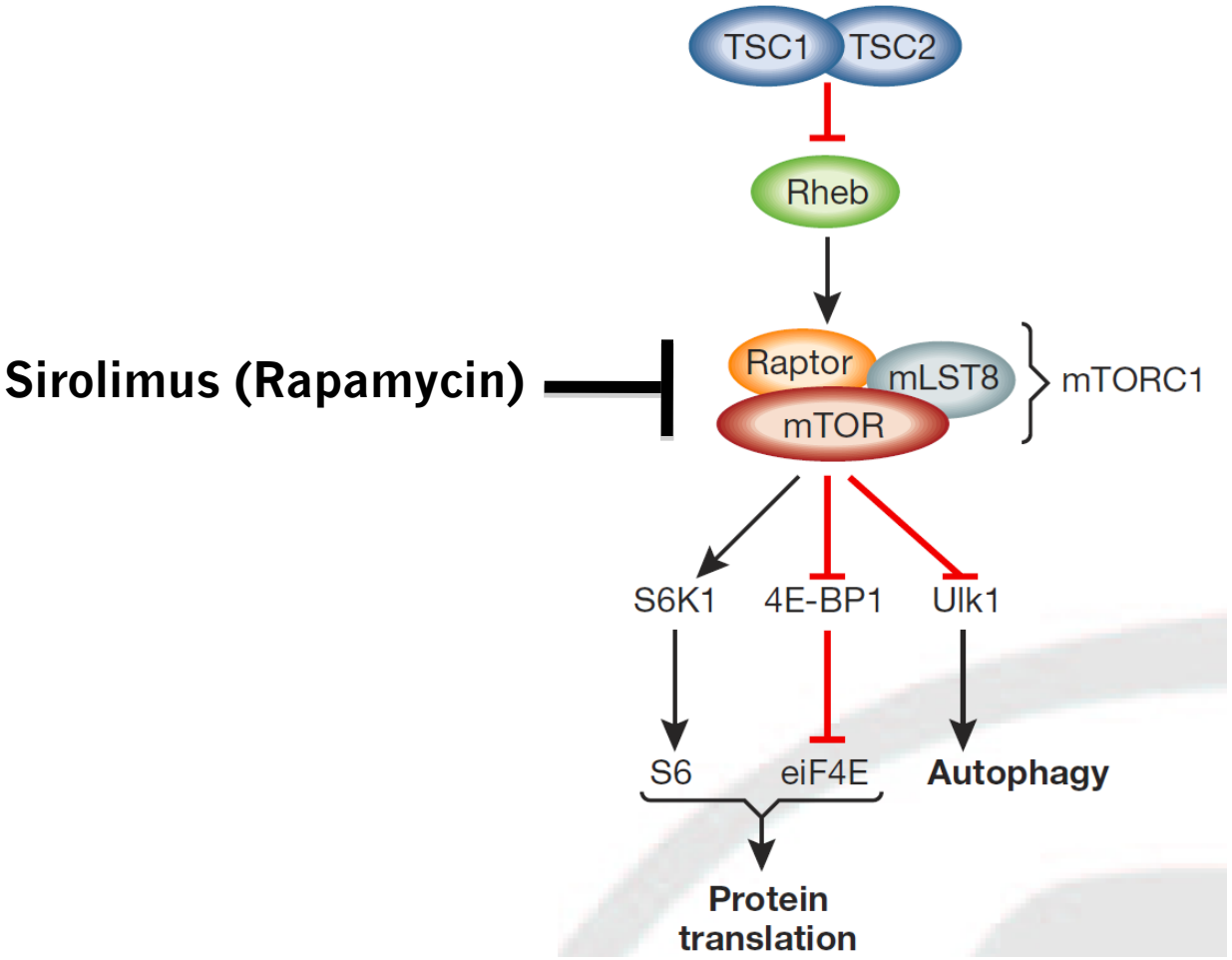
Lung biopsy





Johnson et al. ERJ 2008

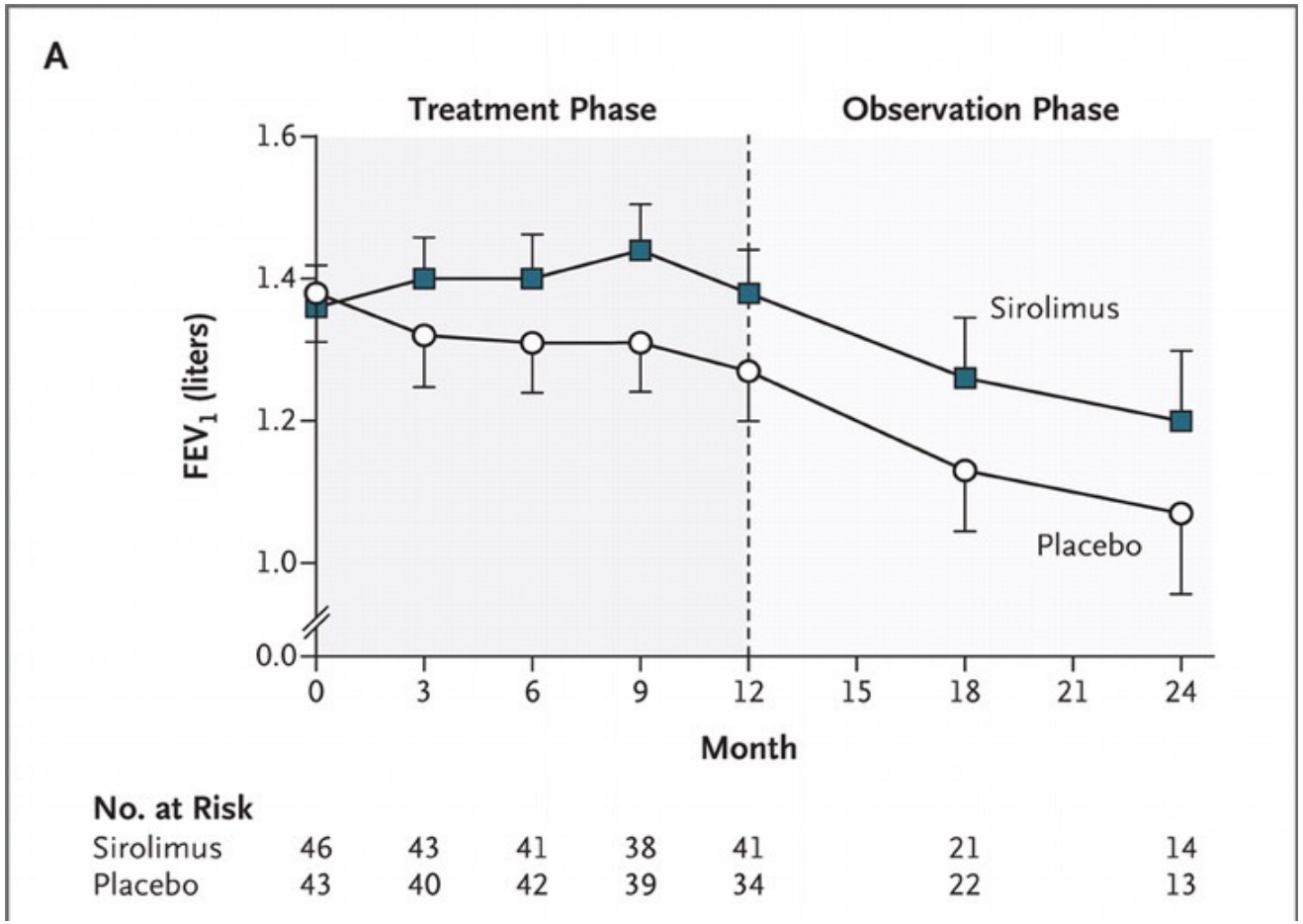
mTOR Kinase is Activated in LAM Cells



Neuman et al. EMBO Molec Med 2011

Rapamycin

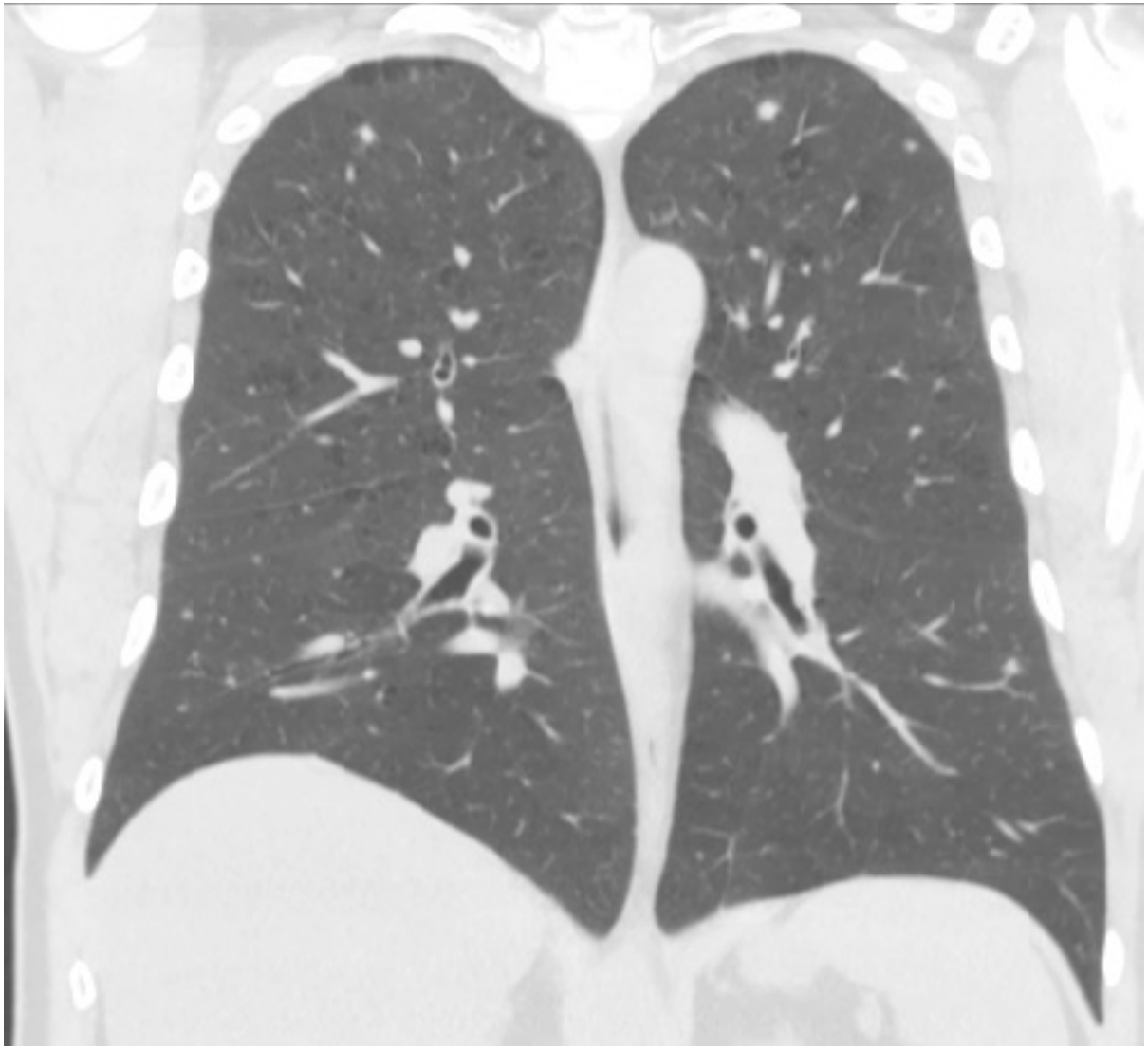
- It works (MILES trial)



McCormack FX et al. N Engl J Med. (2011)

Langerhans cell histiocytosis

Langerhans Cell Histiocytosis



Langerhans Cell Histiocytosis

- Systemic disease or single organ
- Unknown true prevalence (3-5% of all diffuse lung disease?)
- M=F
- >90% smokers
- Cannabis?

Vassallo et al. 2017 Thorax

Adult LCH

- Single or multisystem disease
  - Seborrheic rash
  - Diabetes insipidus
  - HSM/ Lymphadenopathy
- Single site: Most commonly the lungs
  - Smoking history?
  - Polyclonal

Langerhans Cell Histiocytosis

- Lung nodules
- CD1a+ cells (reactive or clonal?)
- Lung destruction
- Smoking

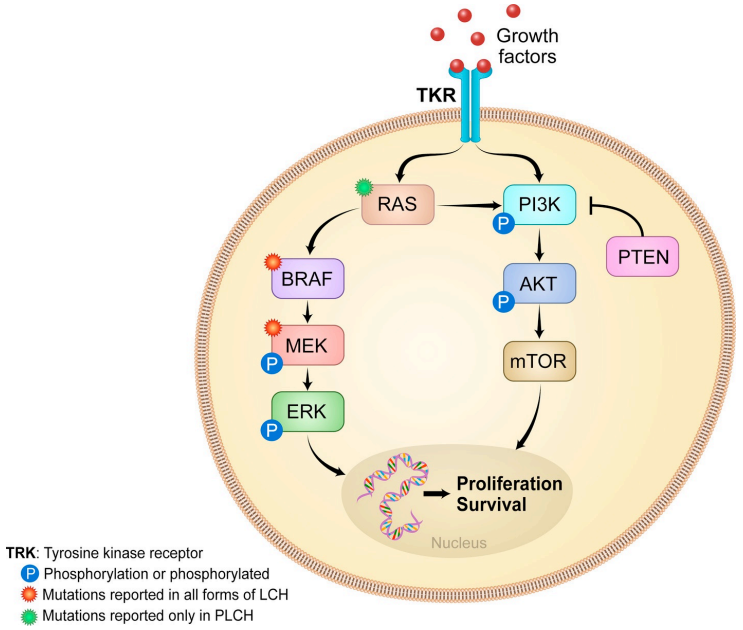
Vassallo et al. 2017 Thorax

PLCH

-Mutations in tumor suppressor gene (BRAF)

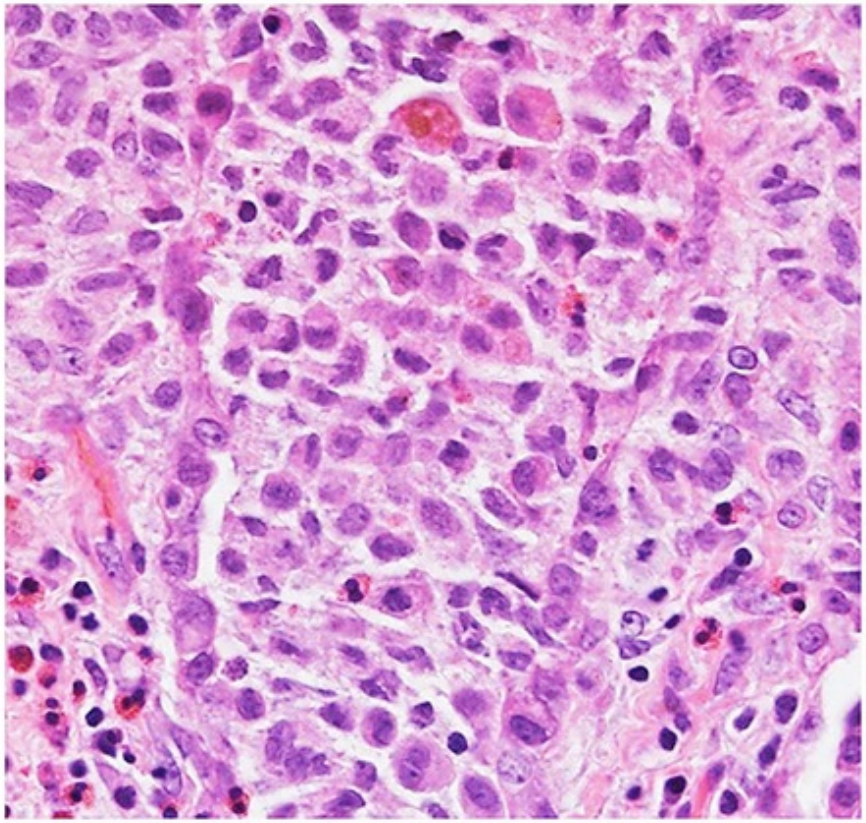
-Potential targeted therapy.

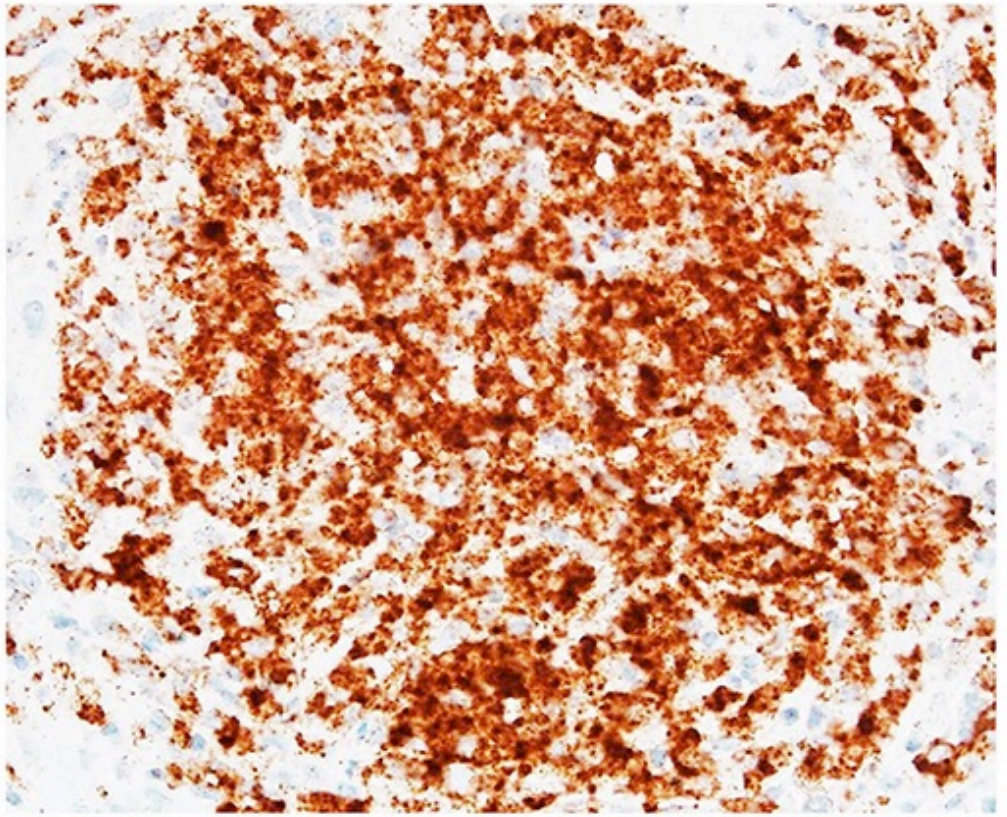
-Circulating cell with mutation in BRAF or NRAS



Vassalo et al. Thorax 2017; Zhang et al. ERJ 2017

Lung biopsy



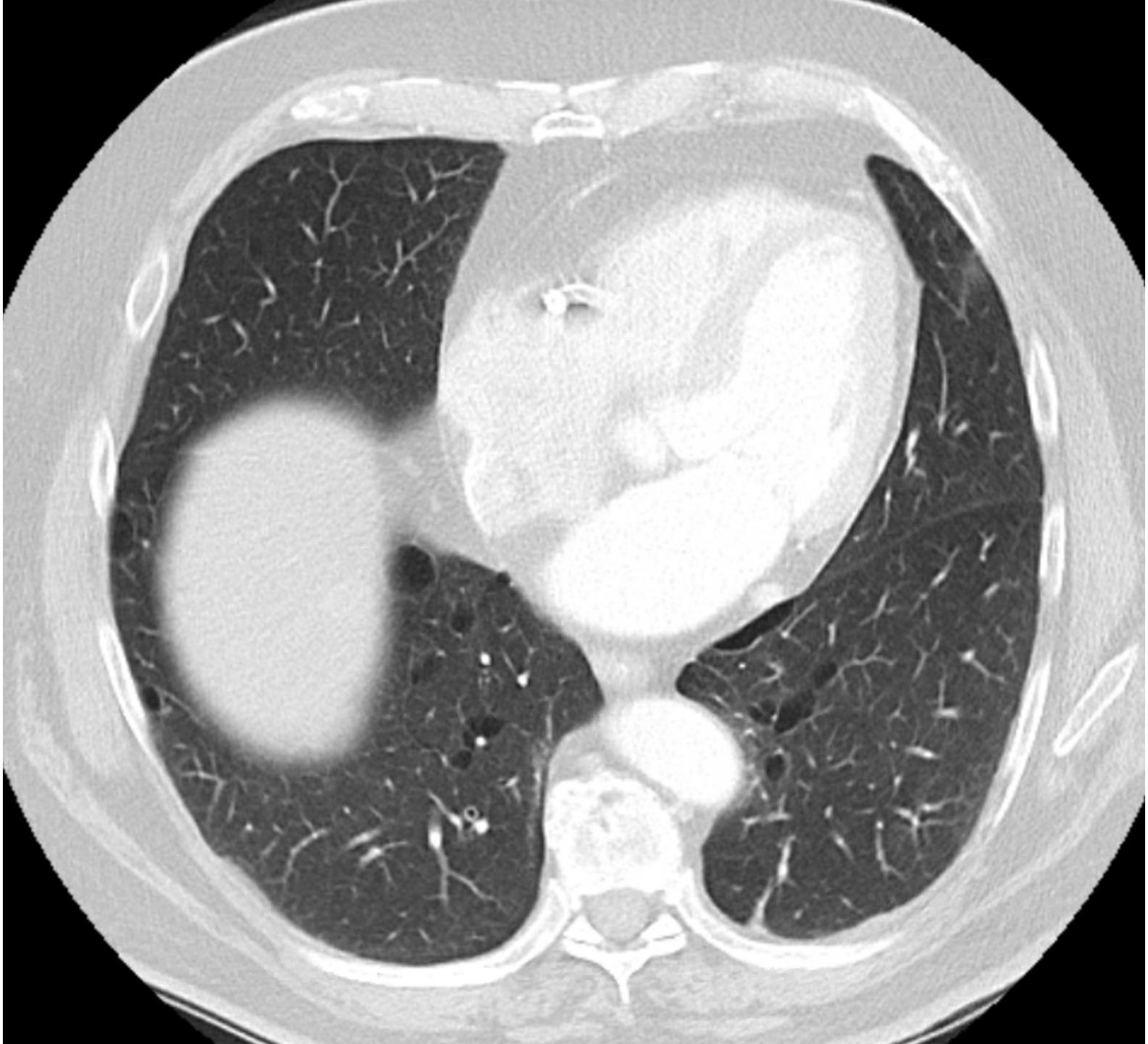


Vassalo et al. Thorax 2017

Treatment and prognosis

- 40-50% spontaneous resolution
- 60% decline over time.
  - Isolated decline in DLCO look for PH
- Smoking cessation

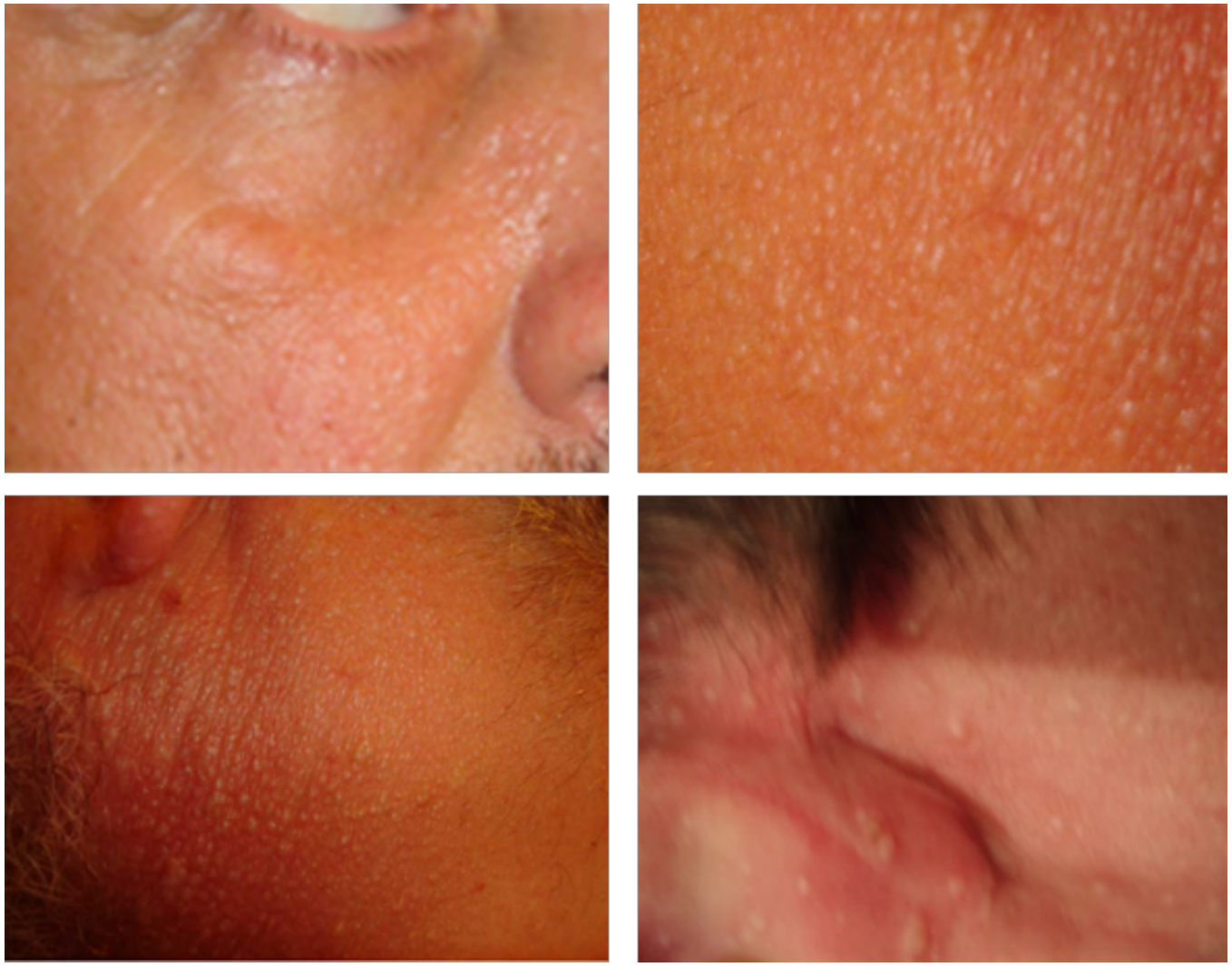
Birt Hogg Dube Syndrome



Birt Hogg Dube

- Autosomal dominant
- Penetrance for lung cysts ~80% by age 50
- 25-75% pneumothorax
- High recurrence rate

Fibrofolliculomas

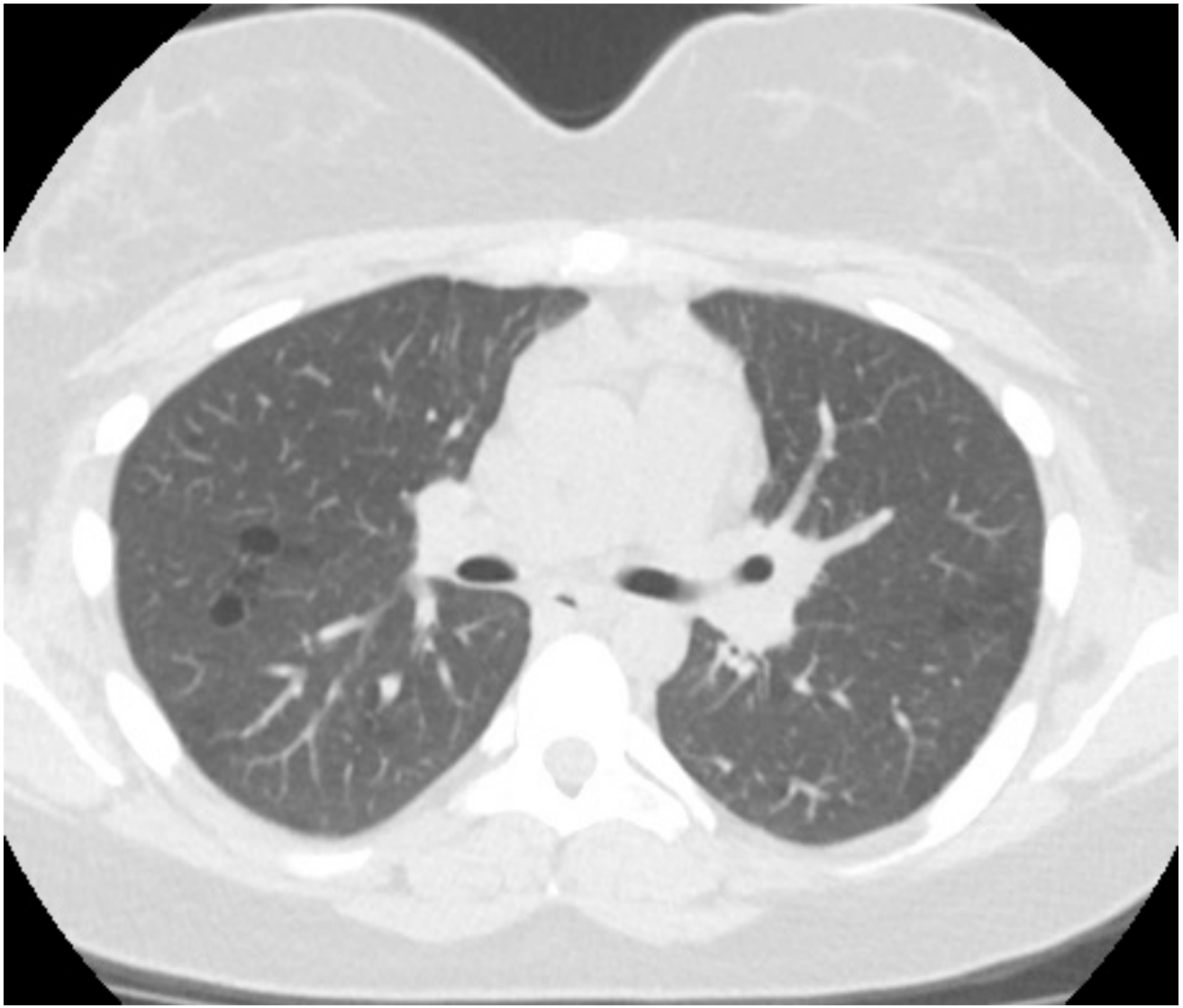


Birt Hogg Dube

- Kidney cancer in ~25%
- Different histological subtypes. Can be bilateral and multifocal
- FLCN gene mutation

Gupta et al. Ann Am Thorac Soc. 2017

Prematurity



Summary

	LAM	PLCH	BHD
HRCT	Round Thin- walled Diffuse	Irregular Sparing angles Nodules	Ellipse Lower lobes pleura
Other features	Women Chylous effusion Angiomyolipoma VEGF-D> 800 pg/ml	Diabetes insipidus Skin and bone lesions	Kidney cancer
Pneumothorax	60%	10-20%	25-75%
Genes	TSC1 or TSC2	BRAF or MEK	FLCN

Question #1

30 years old female presenting with shortness of breath and dyspnea on exertion. Chest radiograph shows a right sided pneumothorax. A CT scan of the chest confirms the presence of pneumothorax and shows cystic lung disease in addition to a fat rich kidney tumor. The treatment is:

a) No need to be concerned about lung function, it will not decline overtime

b) Steroids

c) No available therapies

d) Rapamycin

Question #2

30 years old female presenting with shortness of breath and dyspnea on exertion. Chest radiograph shows a right sided pneumothorax. A CT scan of the chest confirms the presence of pneumothorax and shows cystic lung changes. A careful skin examination shows facial fibrofolliculoma. The next best step

a) Start rapamycin

b) Steroids

c) Lung biopsy

d) CT scan of the abdomen

References

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