Cystic Lung Diseases

Souheil El-Chemaly, MD, MPH
Clinical Director Center for LAM Research and Clinical Care
Division of Pulmonary and Critical Care Medicine
Department of Medicine
Brigham and Women's Hospital

BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S
Department of Medicine

HARVARD MEDICAL SCHOOL
Postgraduate Medical Education

Disclosure

Consulting Sanofi

Learning Objectives

- Identify causes of cystic lung diseases

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

Cystic lung diseases

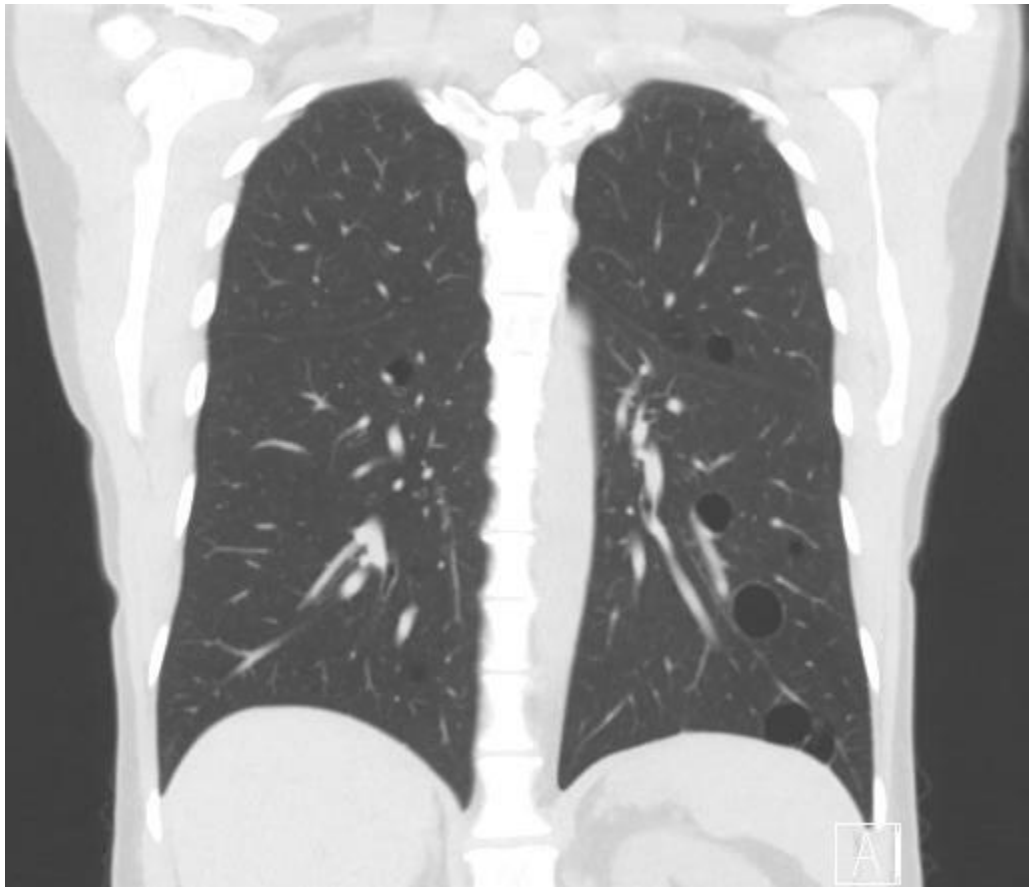
Centrilobular emphysema
Pulmonary metastasis
Subacute (?chronic) hypersensitivity pneumonitis
Desquamative interstitial pneumonia
Barotrauma/ ARDS
Pulmonary infection- pneumatoceles
Necrobiotic nodules
Light chain disease

Lymphangioleiomyomatosis
Langerhans cell histiocytosis
Birt Hogg Dube syndrome
Lymphoid interstitial pneumonia

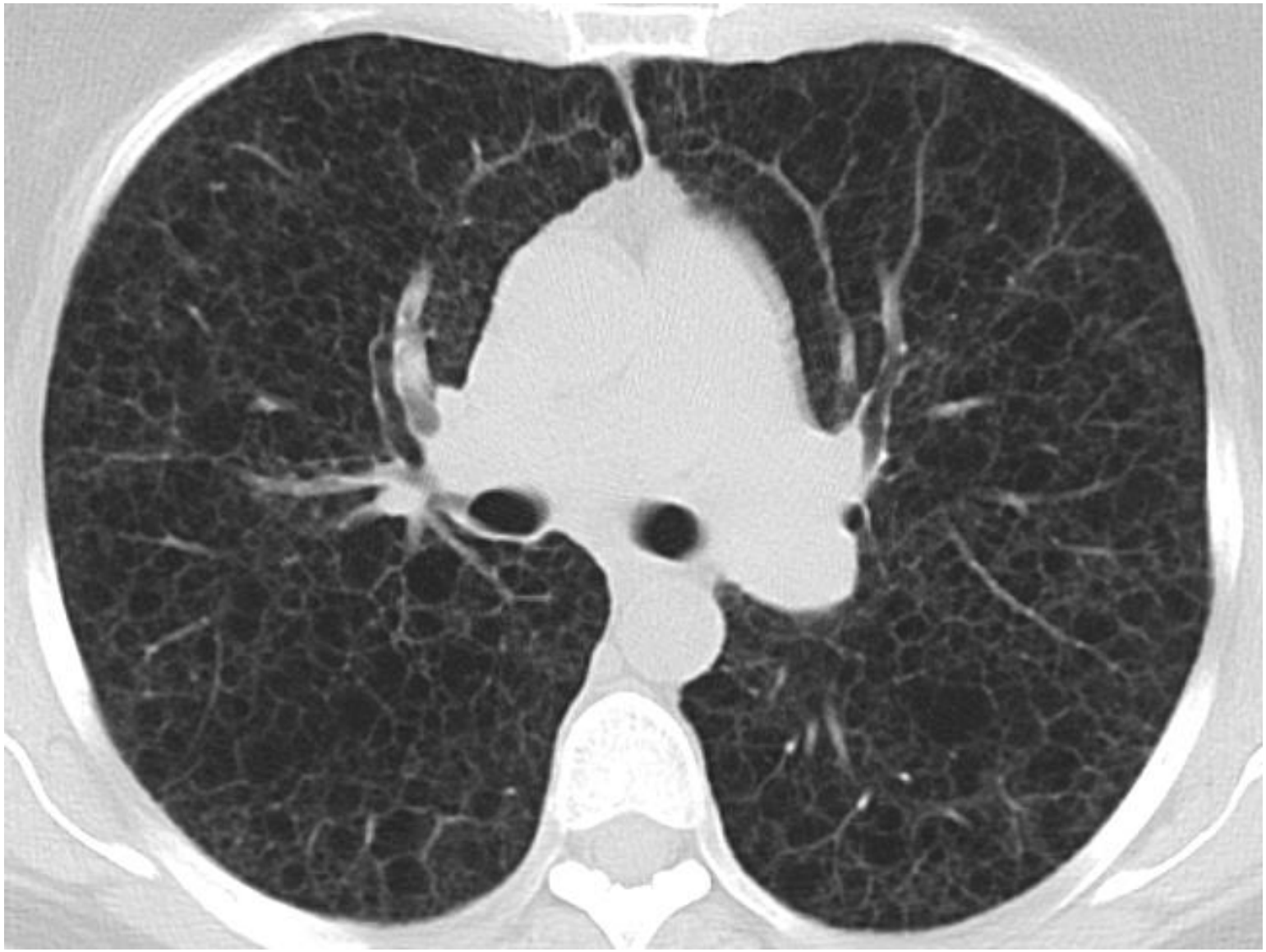
Beddy et al. Insights Imaging 2011 2:1-7

Lymphocytic Interstitial Pneumonia

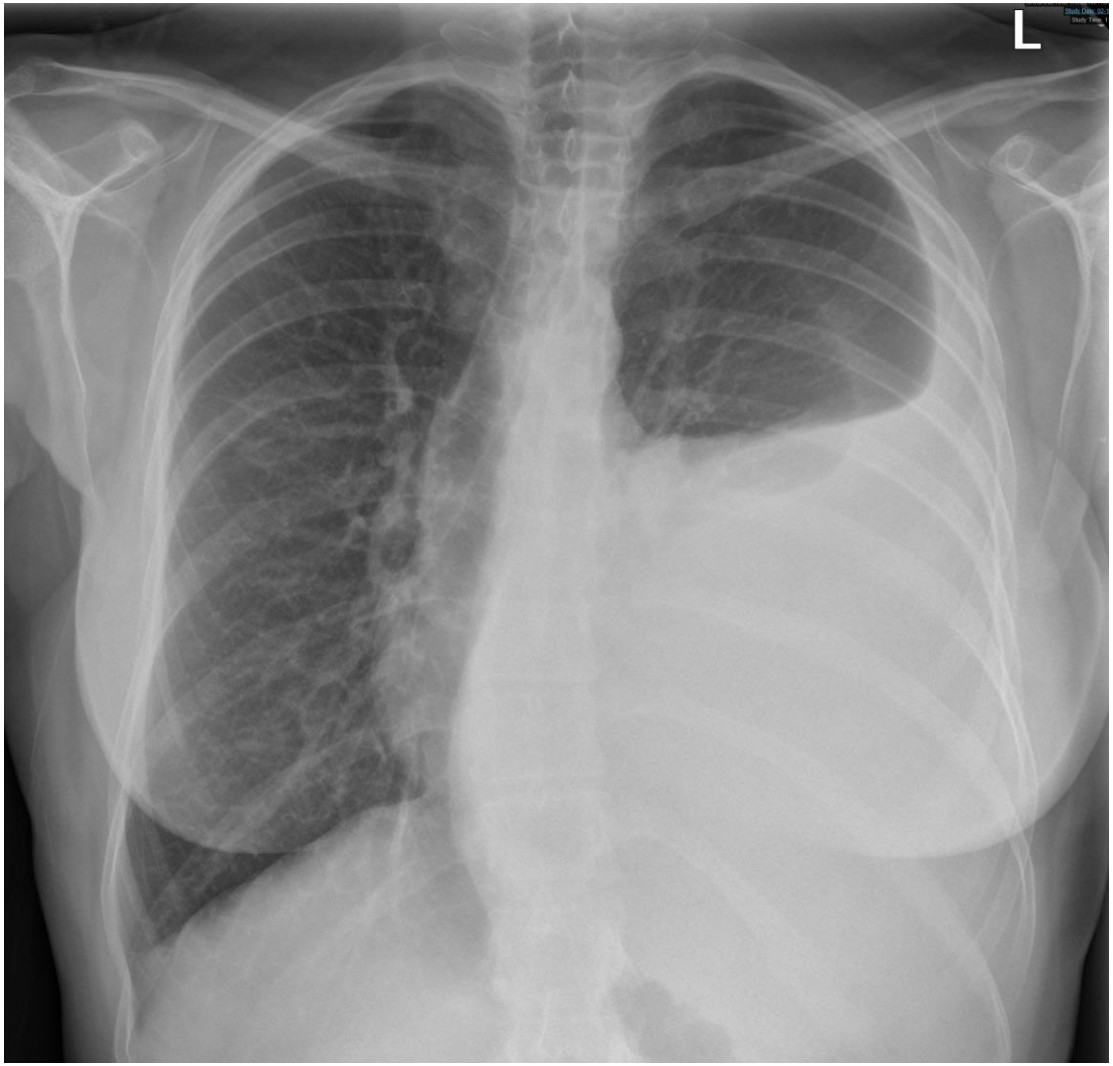
- Associated with connective tissue disease
- Sjogren in 25-50% of LIP cases



Cystic lung changes in LAM



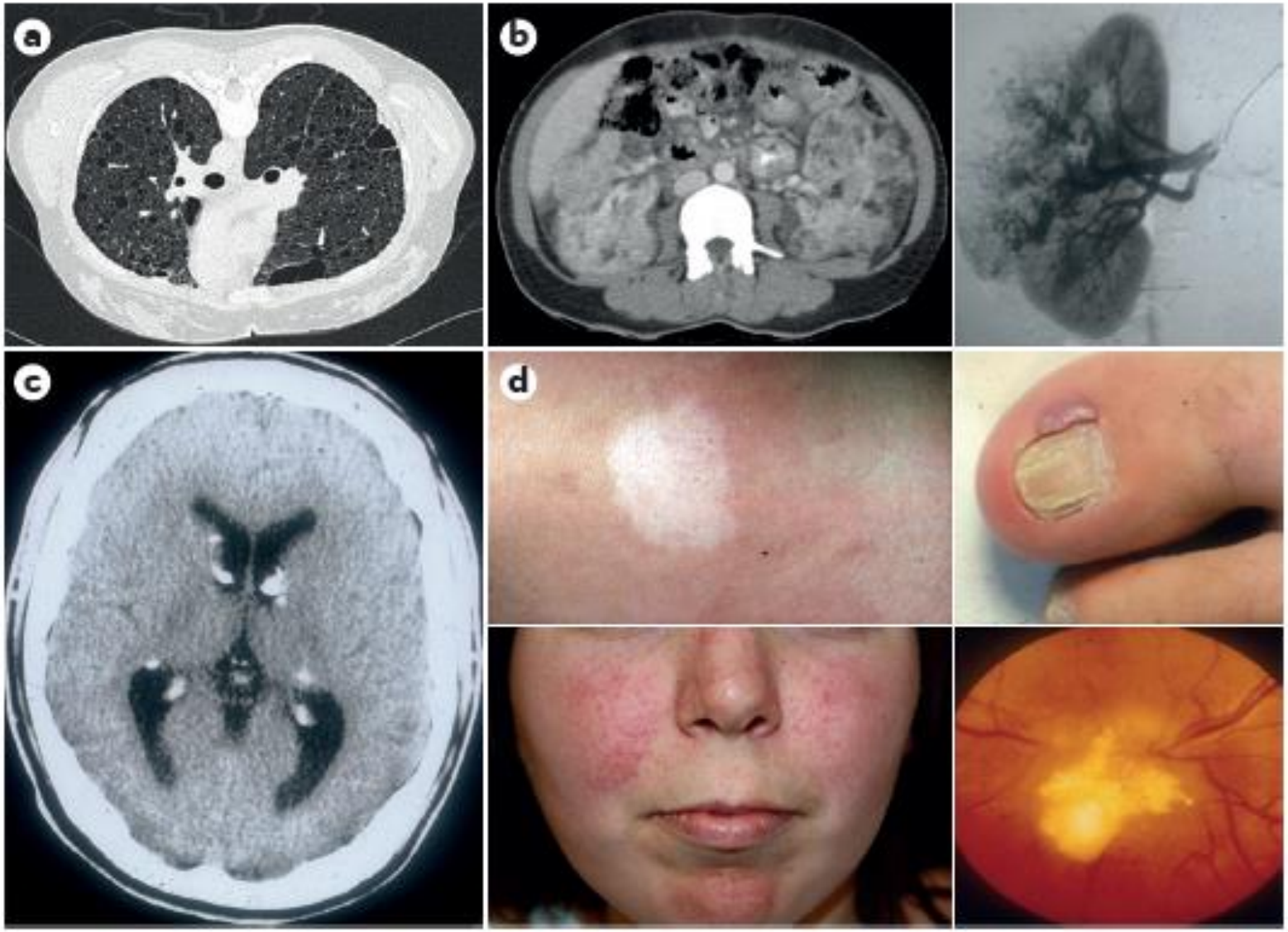
Chylous effusion



Screening for TSC

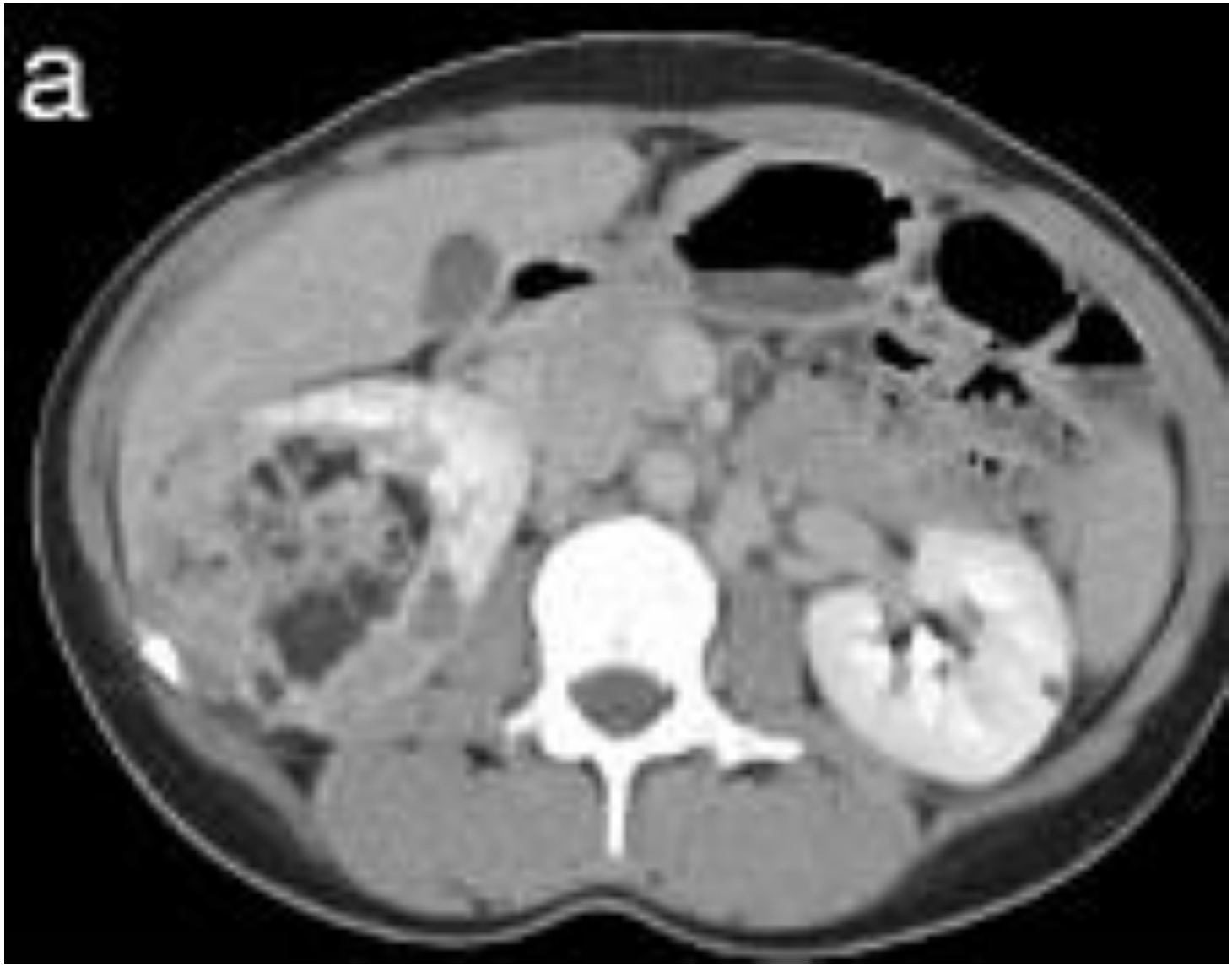
- Personal and family history
- Skin lesions
- Bilateral AML
- Brain lesions

Tuberous Sclerosis Complex



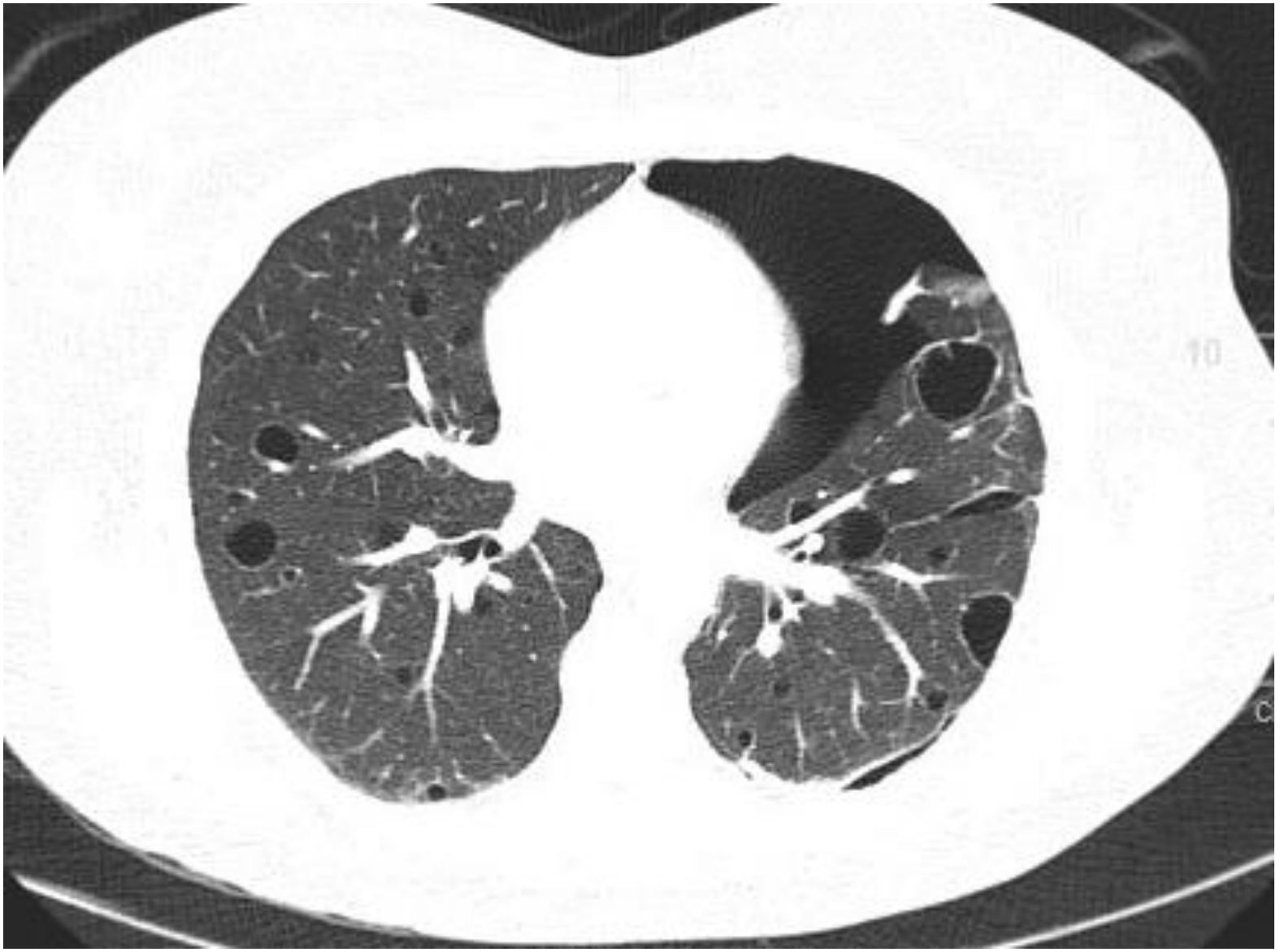
Henske et al. Nature Reviews 2016; Carsillo et al PNAS 2000

Angiomyolipoma (AML)



Yeoh et al. 2014 Orphanet Journal of Rare Diseases

Pneumothorax

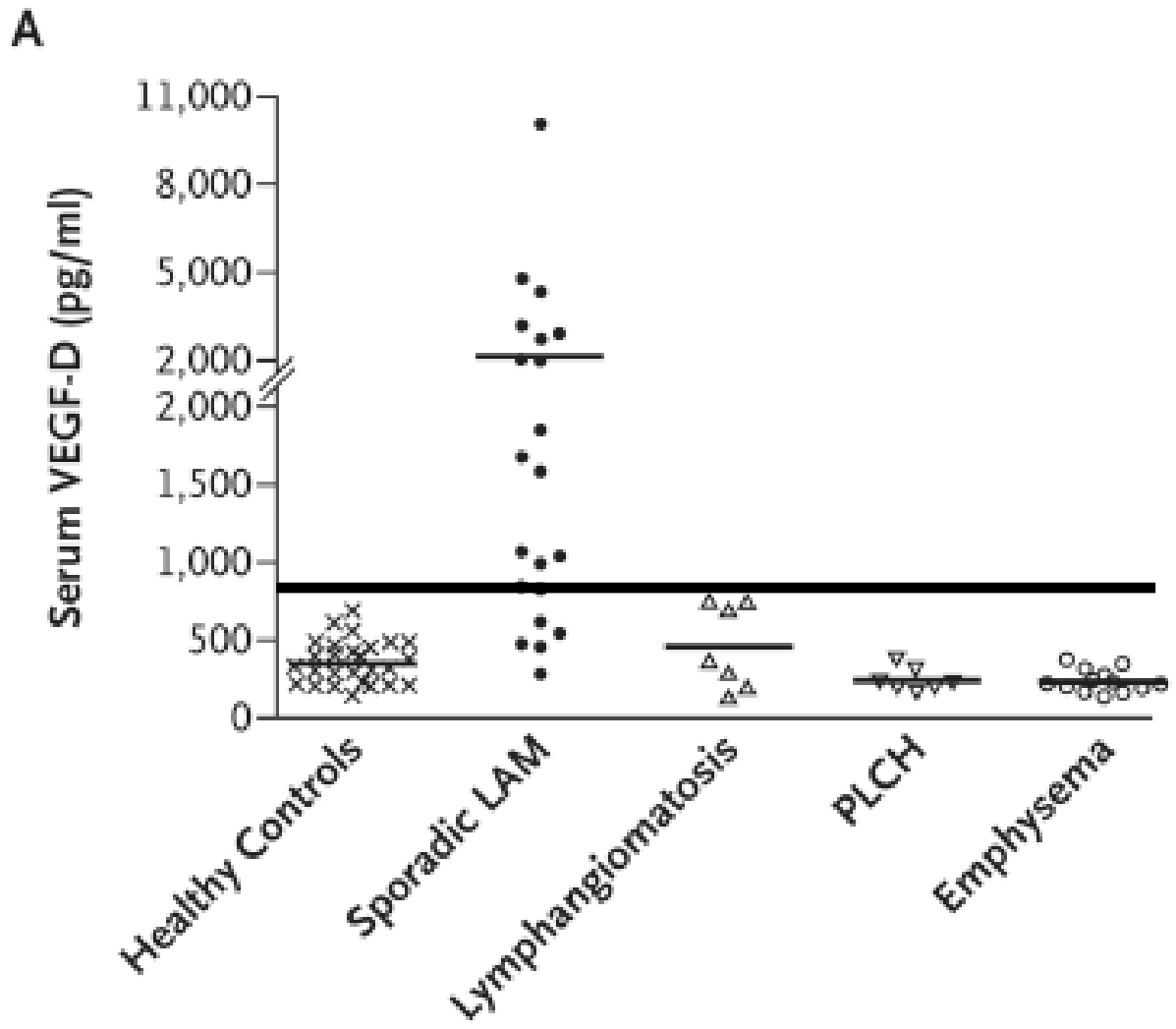


Pneumothorax

- 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

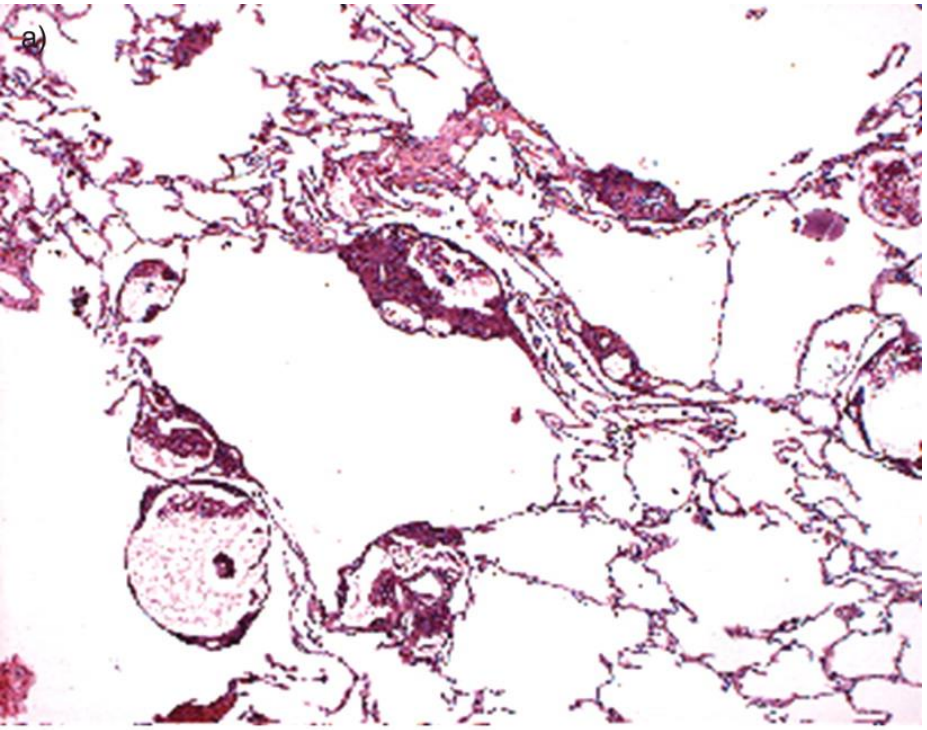
- Typical cystic changes

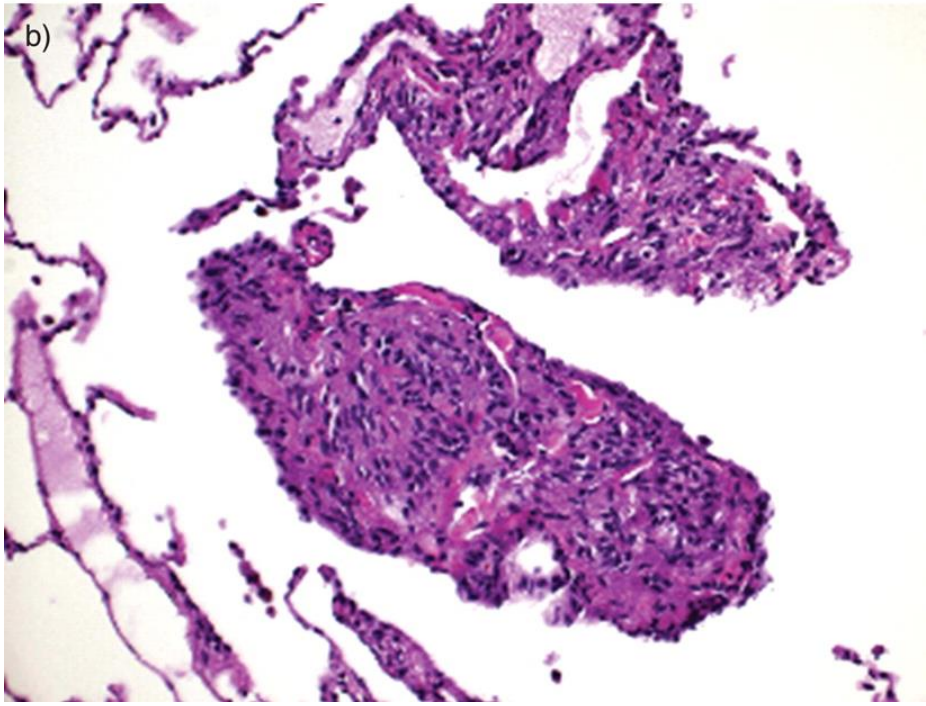
+ any

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

McCormack et al. Am J Respir Crit Care Med 2016

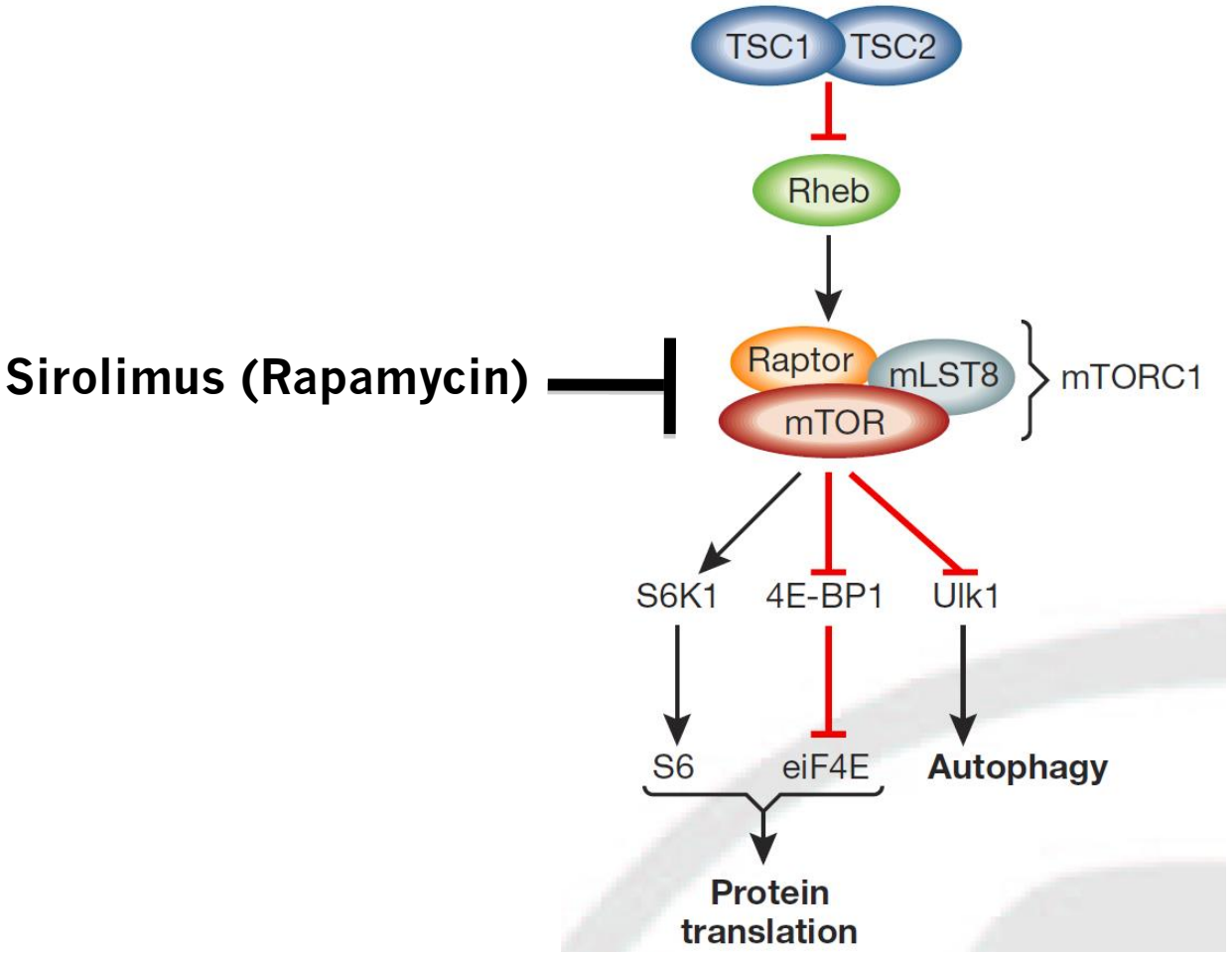
Lung biopsy





Johnson et al. ERJ 2008

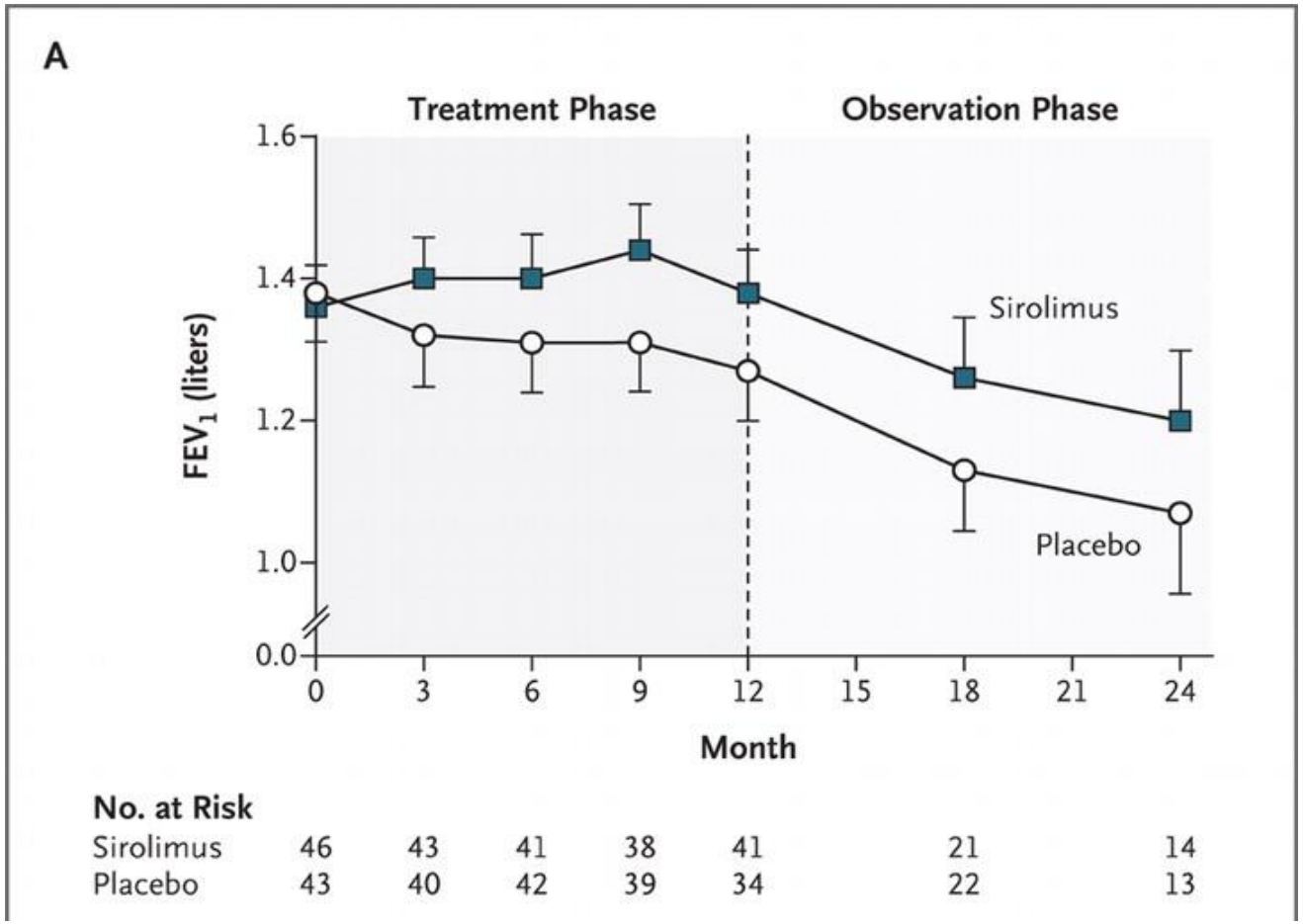
mTOR Kinase is Activated in LAM Cells



Neuman et al. EMBO Molec Med 2011

Rapamycin

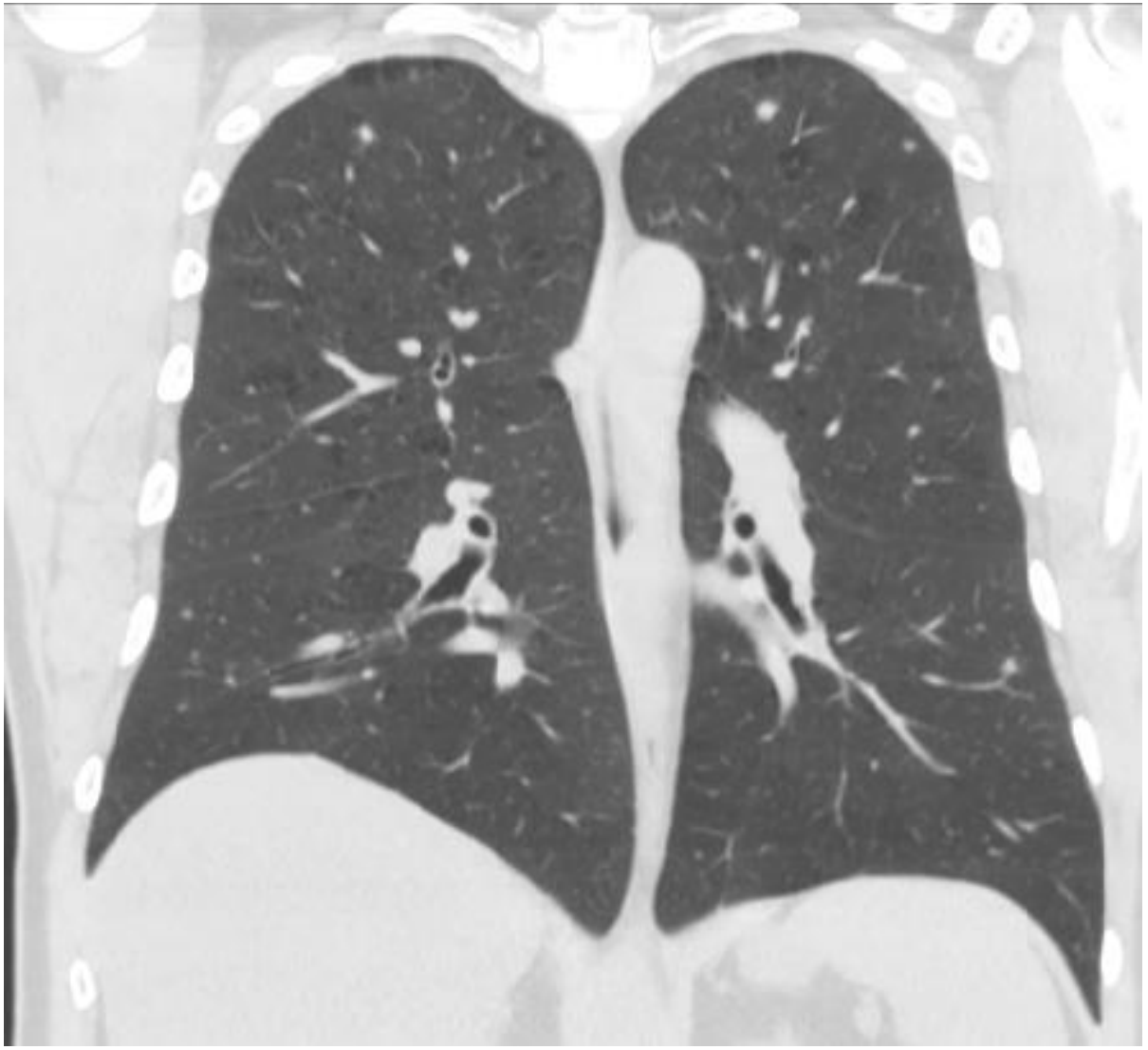
- It works (MILES trial)



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
- Lung destruction
- Smoking

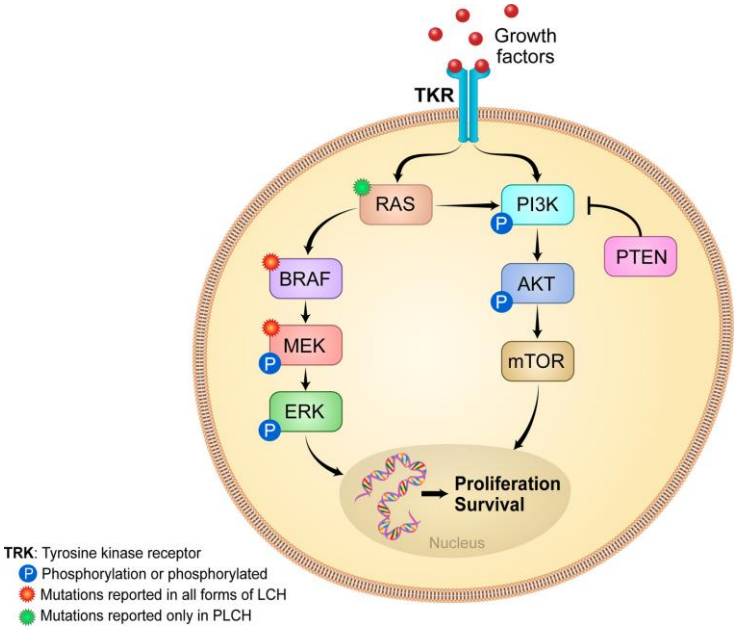
Vassallo et al. 2017 Thorax

PLCH

-Mutations in tumor suppressor gene (85% MAPK and 35-50% in BRAF)

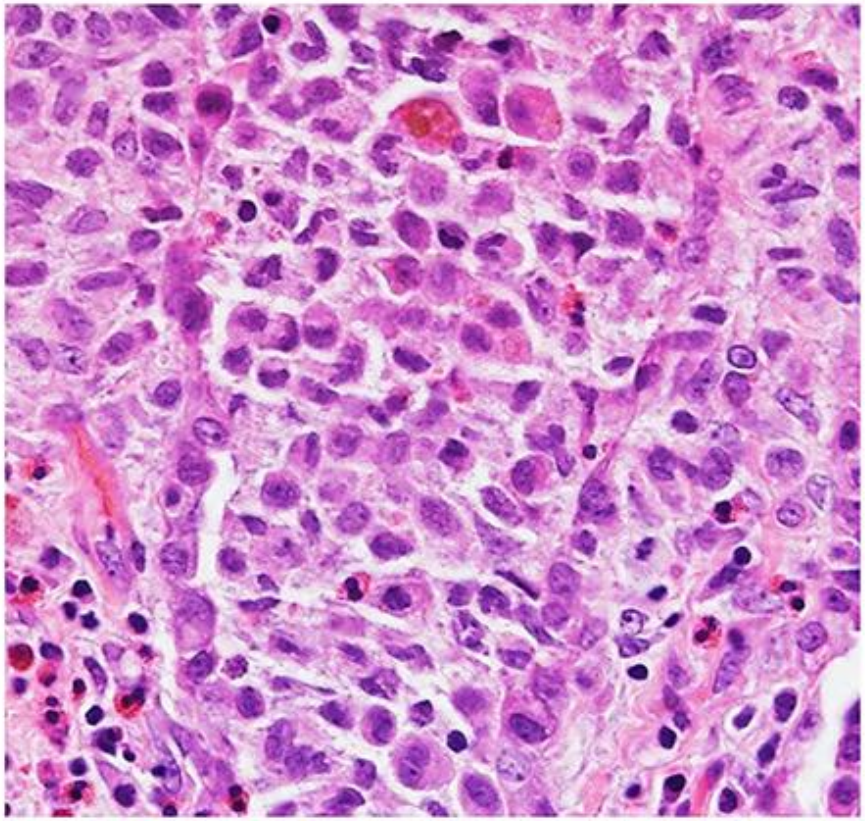
-Potential targeted therapy.

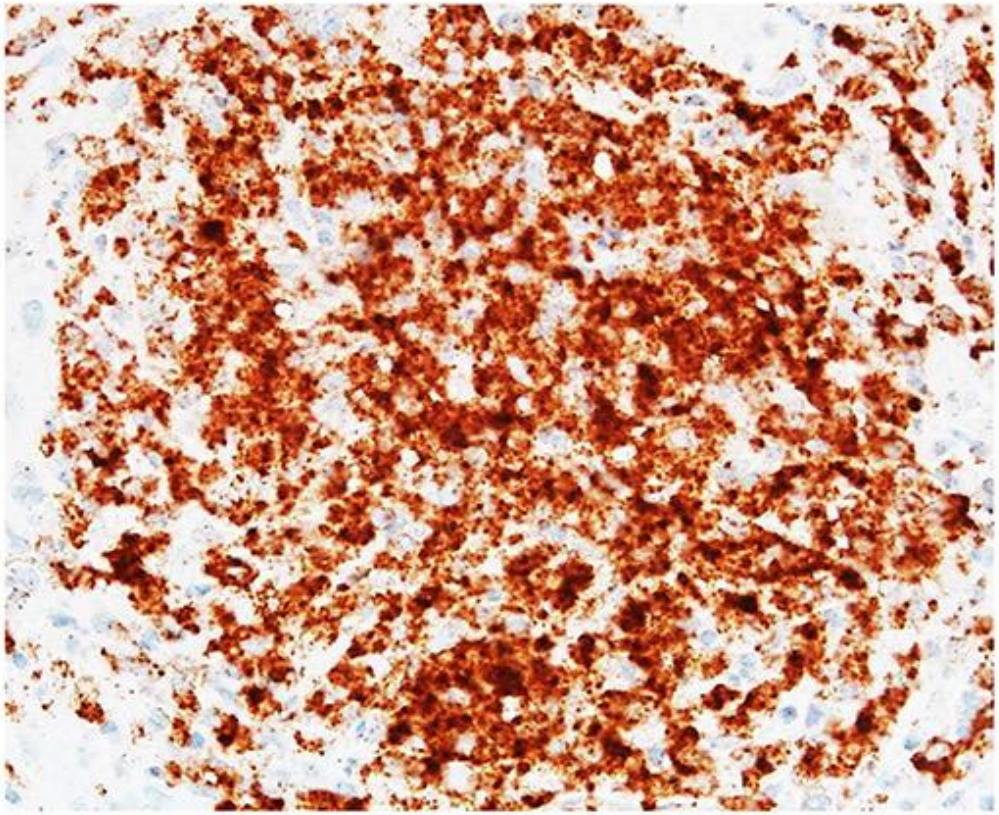
-Circulating cell with mutation in BRAF or NRAS



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

Lung biopsy



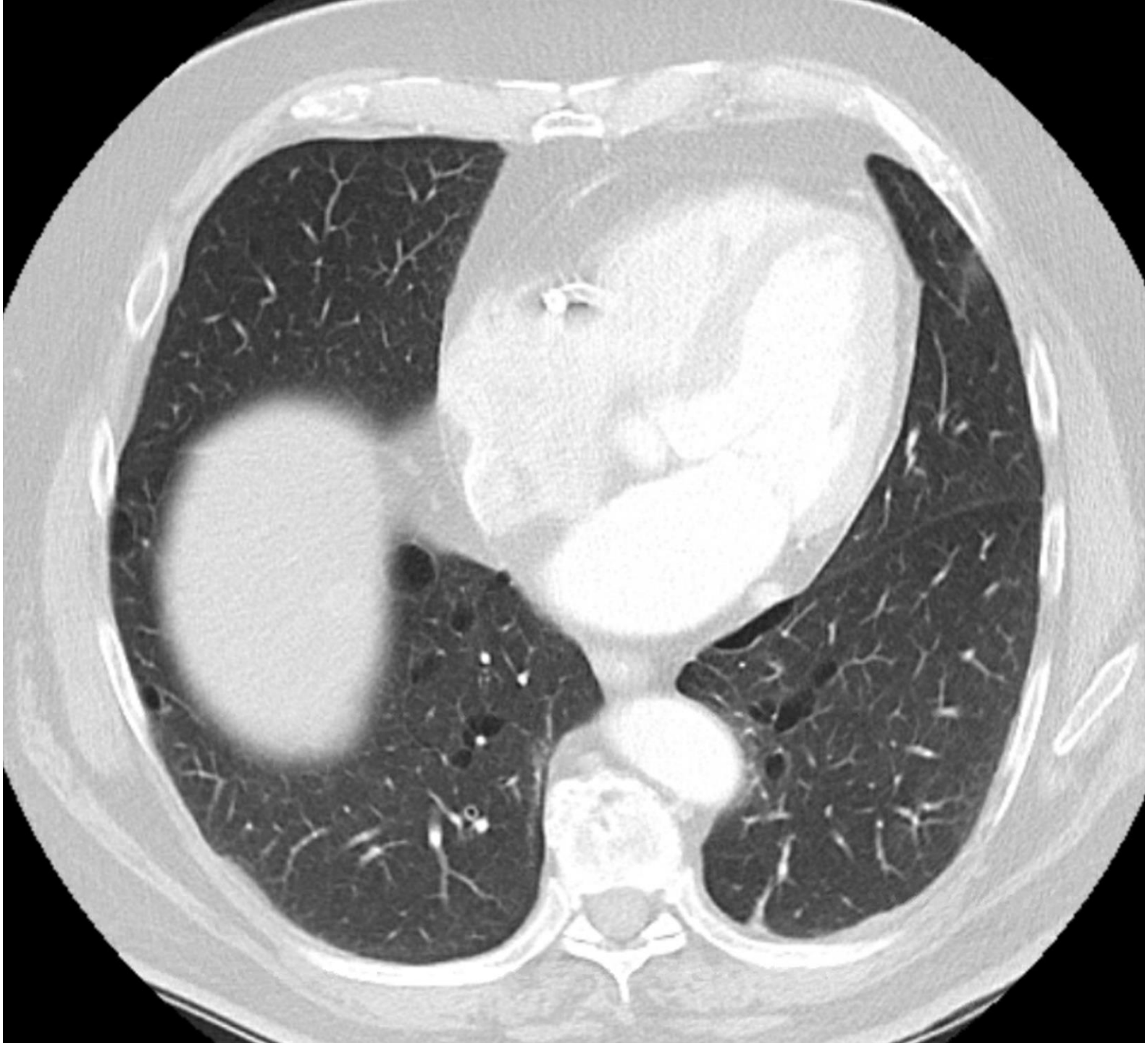


Vassalo et al. Thorax 2017

Treatment and prognosis

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

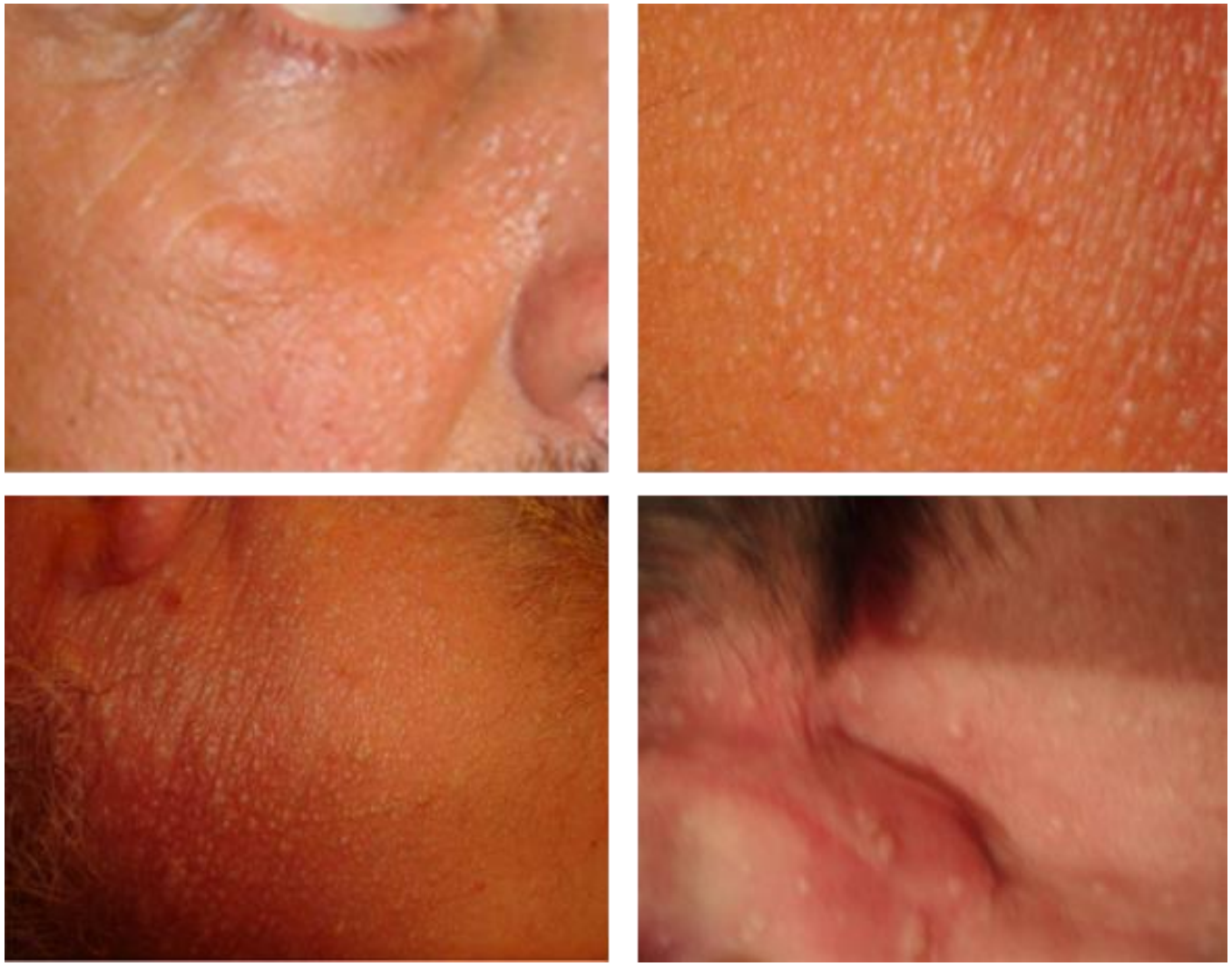
Birt Hogg Dube Syndrome



Birt Hogg Dube

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

Fibrofolliculomas



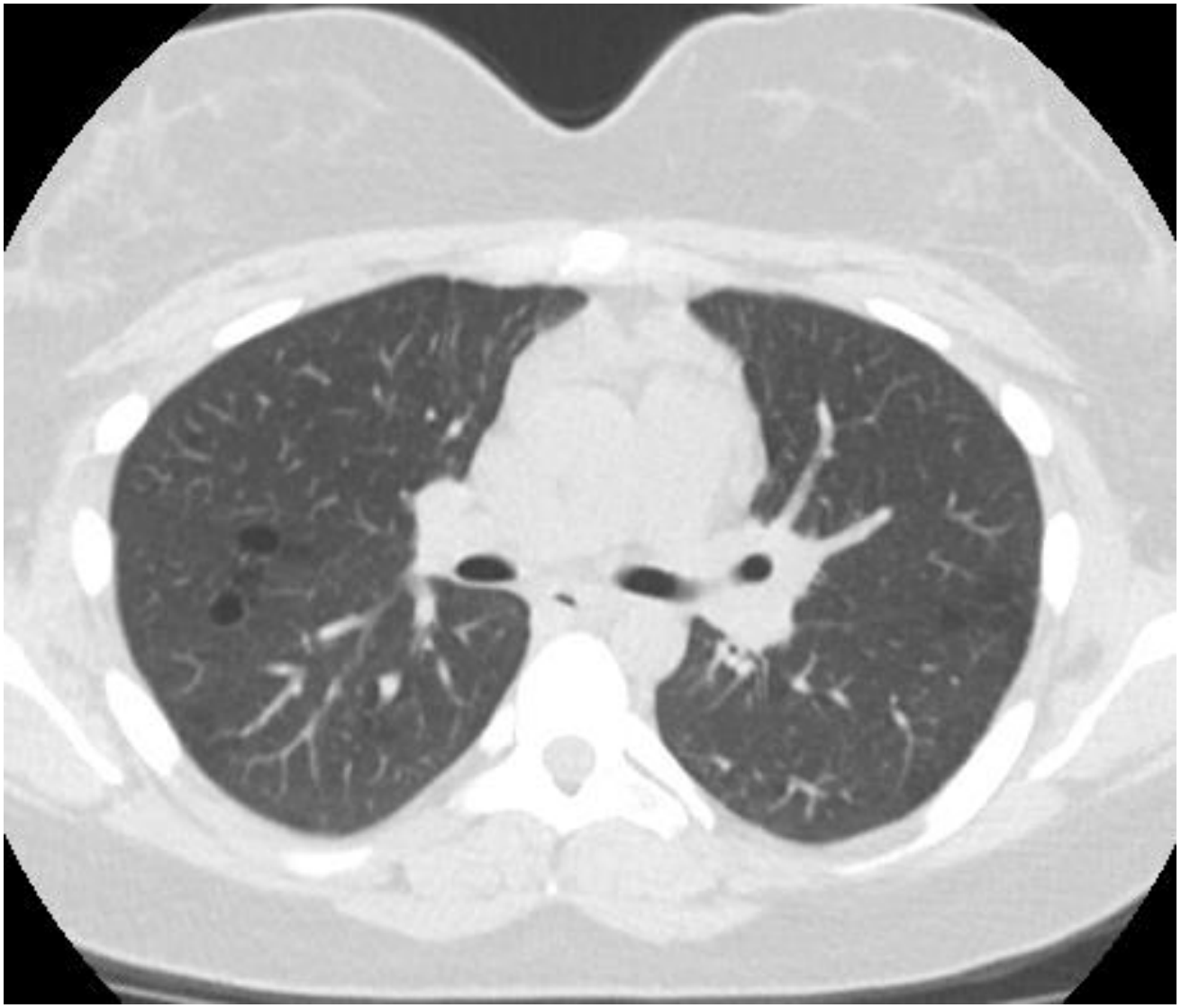
BHDsyndrome.org

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 #1

Answer d) Rapamycin.

This is a patient who has LAM. The presence of cystic lung disease and an angiomyolipoma is diagnostic of LAM. In this setting there is no need for a lung biopsy. Other features that could have confirmed the diagnosis are the presence of chylous effusions and a high VEGF-D level (>800pg/ml).

If a patient with LAM requires therapy, the treatment as an mTOR inhibitors such as rapamycin. This has been shown in the MILES trial.

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

Question #2

d) CT scan of the abdomen. This patient has BHD. The presence of facial fibrofolliculoma is pathognomonic of BHD. The major risk in BHD is renal cell carcinoma. A CT scan of the abdomen should be obtained to screen for kidney tumors. BHD

References

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