A New Path to Medicine

Current Treatment Options for Pulmonary Sarcoidosis

Key Opinion Leader Event

June 29, 2021

Forward Looking Statements

The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” “opportunity,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements regarding: the potential therapeutic benefits of proteins derived from tRNA synthetase genes and our product candidates, including ATYR1923 and ATYR2810, and development programs, including our NRP2 antibody program and our tRNA synthetase program; the ability to successfully advance our product candidates and undertake certain development activities (such as the initiation of clinical trials, clinical trials enrollment, the conduct of clinical trials and announcement of clinical results) and accomplish certain development goals, and the timing of such events; the potential market opportunity for our product candidates; our ability to receive regulatory approvals for, and commercialize, our product candidates; our ability to identify and discover additional product candidates; potential activities and payments under collaboration agreements; and the ability of our intellectual property portfolio to provide protection are forward-looking statements. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These risks, uncertainties and other factors are more fully described in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, and in our other filings. The forward-looking statements in this presentation speak only as of the date of this presentation and neither we nor any other person assume responsibility for the accuracy and completeness of any forward-looking statement. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

aTyr Pharma

Corporate Overview

aTyr: A New Path to Medicine

Mission: Develop a new class of medicines based on proprietary biology platform with a novel approach for identifying target receptors for extracellular tRNA synthetase fragments from an IP portfolio covering protein derivatives from all 20 tRNA synthetase gene families

ATYR1923

- Immunomodulator for severe inflammatory lung diseases
- Pulmonary sarcoidosis trial enrollment completed – data expected Q3 2021
- Positive results reported in COVID-19 pts in Q1 2021

NRP2 Antibodies

- ATYR2810: lead anti-neuropilin-2 (NRP2) antibody for cancer – IND-enabling activities initiated
- NRP2 antibody research program for distinct therapeutic applications

tRNA Synthetase Candidates

- Receptors identified for two new tRNA synthetases from our pipeline
- Discovery programs targeting NK cell biology

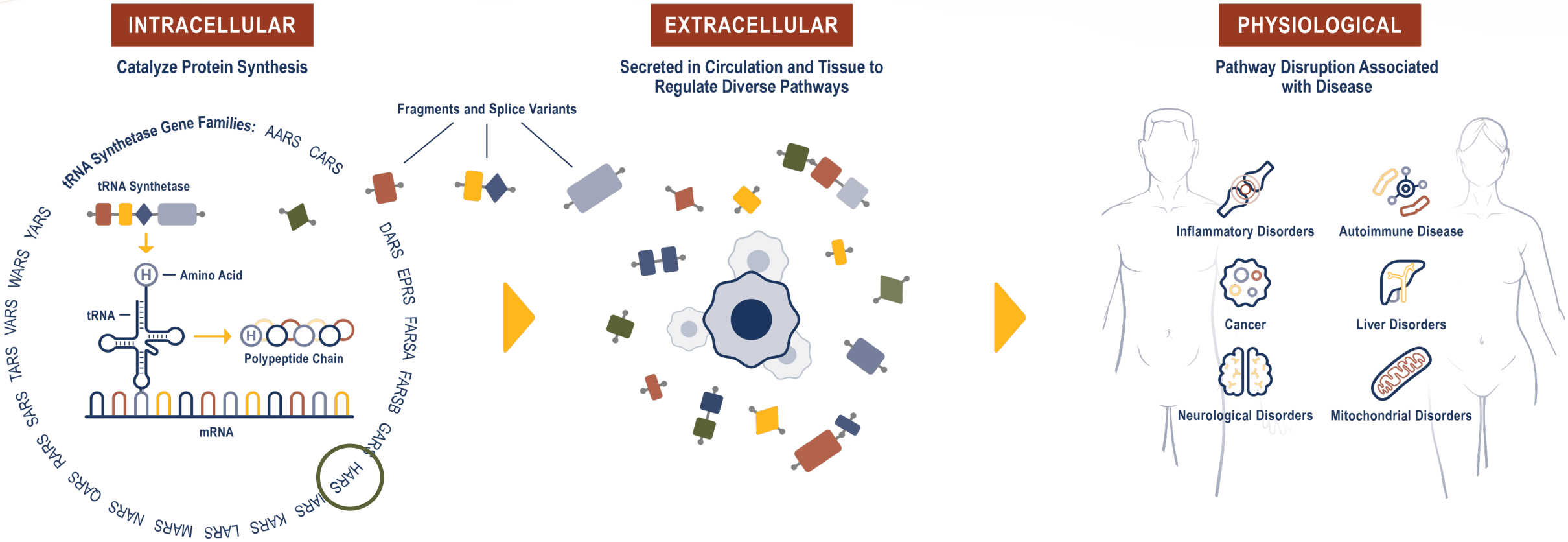
Financials: Cash, cash equivalents and investments at $50.6m as of March 31, 2021

aTyr Development Pipeline

PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
ATYR1923	Pulmonary Sarcoidosis					
	Other ILDs (CTD-ILD; CHP)(1)					
	Healthy Japanese Volunteers(2)					
	COVID-19 related severe respiratory complications					
ATYR2810	Solid Tumors					
NRP2 mAbs	Cancer; Inflammation					
AARS-1; DARS-1(3)	Cancer; Fibrosis; Inflammation					

(1) CTD-ILD: connective tissue disease-related ILD (e.g. Scleroderma-related ILD); CHP: chronic hypersensitivity pneumonitis
(2) In partnership with Kyorin Pharmaceutical Co., Ltd.
(3) The next two candidates from our tRNA synthetase platform; initial focus on NK cell biology

tRNA Synthetases May Have Novel Functions Extracellularly



tRNA synthetases are secreted extracellularly and occur in novel forms which lose their canonical function

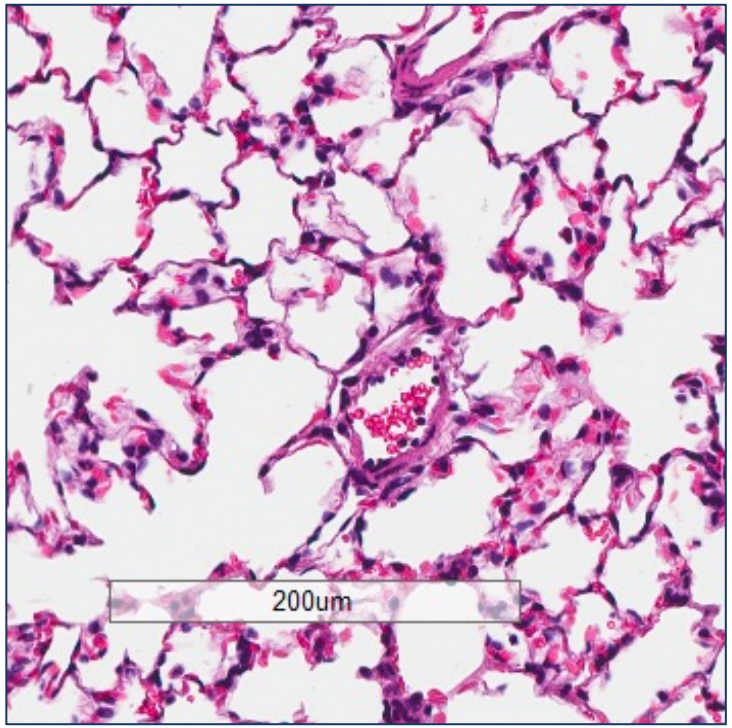
Extracellular tRNA synthetase disruption (genetic/ autoimmune) is associated with disease in humans

ATYR1923

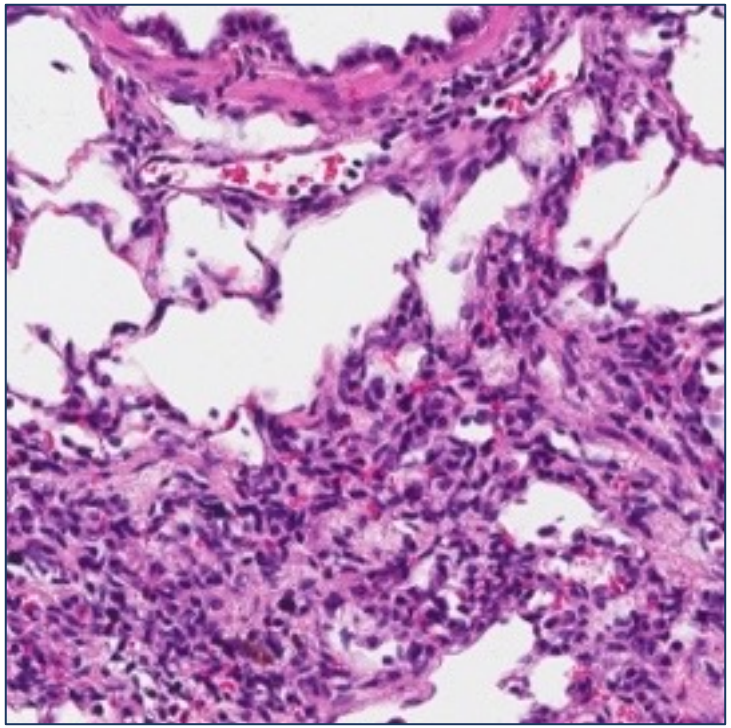
A Novel Immunomodulator for Inflammatory Lung Disease

A Novel Mechanism to Treat Inflammation

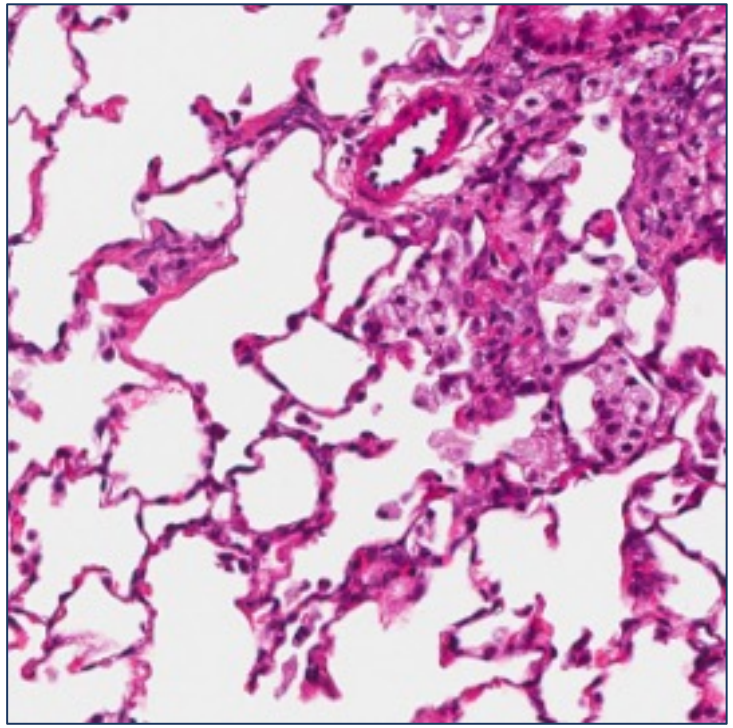
Healthy lung



Injured lung



ATYR1923 treated



Representative histology showing immune cell infiltrate in a rat model of bleomycin induced lung fibrosis presented at the American Thoracic Society annual meeting 2018.

ATYR1923: Early Data Supports Therapeutic Potential in Immune-Mediated Lung Disease

MOA	• Fc fusion protein, based on naturally occurring splice variant of the lung-enriched histidyl-tRNA synthetase (HARS) fragment • Binds to NRP2, a cell surface receptor upregulated on key immune cells during inflammation • NRP2 expression is enriched in inflamed lung tissue, including lung granulomas associated with human sarcoidosis of the lung and skin and lung tissue from patients who died from COVID-19 related respiratory failure
Safety	• Phase 1 study in healthy volunteers PK supports with once-monthly IV dosing • Generally safe and well-tolerated in patients and subjects dosed to date with exposure up to 24 weeks • Two independent DSMB reviews from Ph 1b/2a study in pulmonary sarcoidosis • Positive safety findings from Phase 2 study in COVID-19 severe respiratory symptoms
Efficacy	• Downregulates inflammatory and pro-fibrotic cytokine and chemokine levels and histological inflammation and fibrosis in pre-clinical models • Reduces inflammatory cytokine levels in patients consistent with preclinical models, including cytokines implicated in sarcoidosis and other ILD • Proof-of-mechanism from biomarker data in Phase 2 study in patients with COVID-19

Demonstrated Effect in Animal Lung Injury Models

P. acnes (Sarcoidosis)	↓ pro-fibrotic proteins
S. Rectivirgula (CHP)	↓ tissue cytokines/chemokines and enzymes
Sclerodermatous GvHD (SSc-ILD)	↓ fibrosis
SKG mice (RA-ILD)	↓ immune infiltrates
Bleomycin-Induced Lung Fibrosis (IPF)	↓ inflammation / fibrosis

Consistent downregulation of pro-inflammatory cytokines including IL-6, MCP-1, and IFN-γ

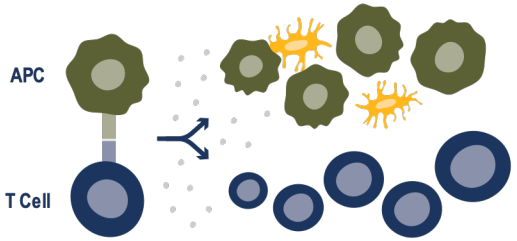
Data available at https://www.atyrpharma.com/our-science/publications/

ATYR1923 Mechanism of Action in Inflammatory Lung Disease

Disease Trigger

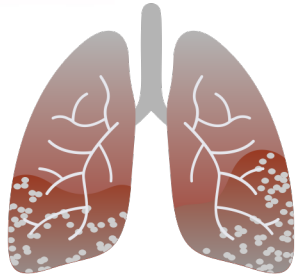
Organic; inorganic; infectious; autoimmune

Aberrant Immune Responses



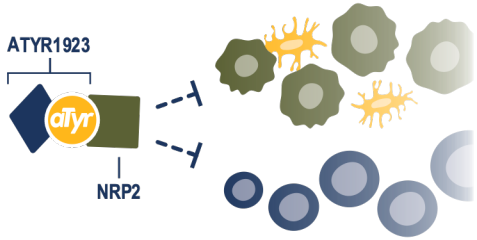
T-cell activation; Pro-inflammatory cytokine/chemokines triggering fibrotic pathways; NRP2 upregulation on immune cells

Lung Inflammation & Fibrosis



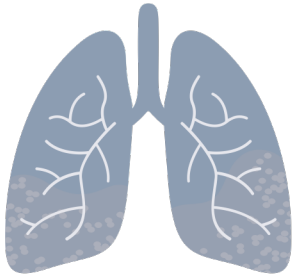
Persistent, unresolved inflammation in the lung can lead to fibrosis; patients experience chronic cough, dyspnea, mortality

ATYR1923 Dampens Immune Responses



ATYR1923 binds to NRP2 and downregulates cytokine and chemokine production and T-cell activation

Stabilized Lung



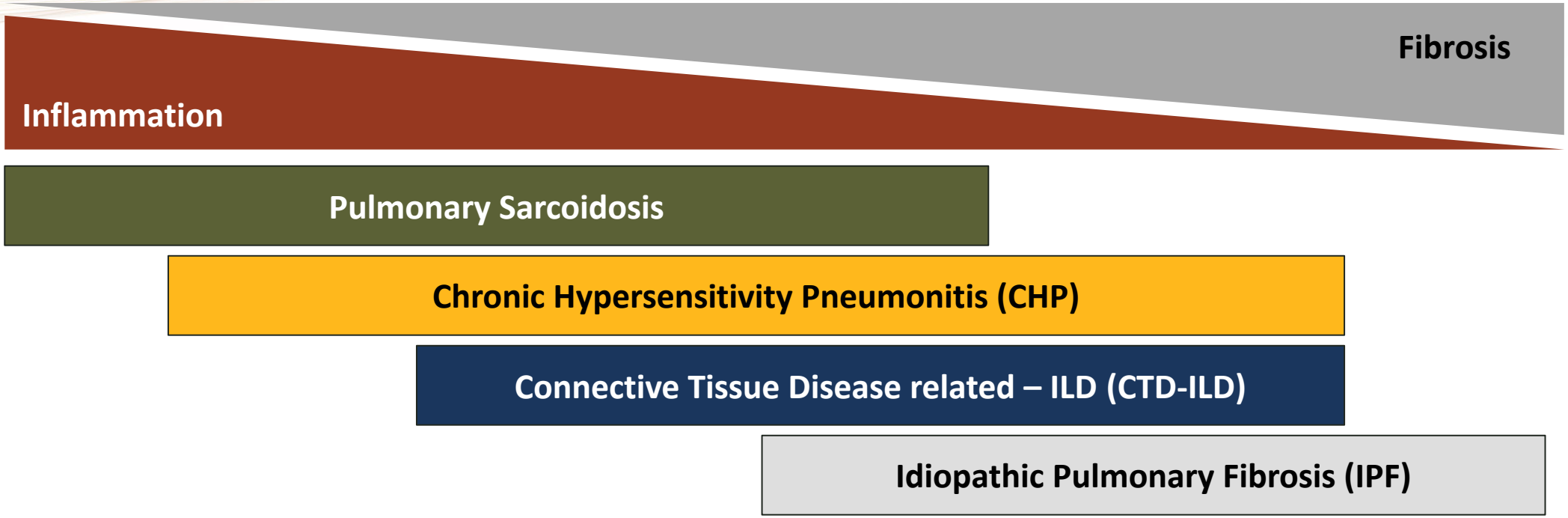
Reduced inflammation and fibrotic deposition; symptom relief, stabilized lung function*

*aTyr hypothesis

ATYR1923

Interstitial Lung Disease

ILDs Share Common Immune Pathology Leading to Fibrosis

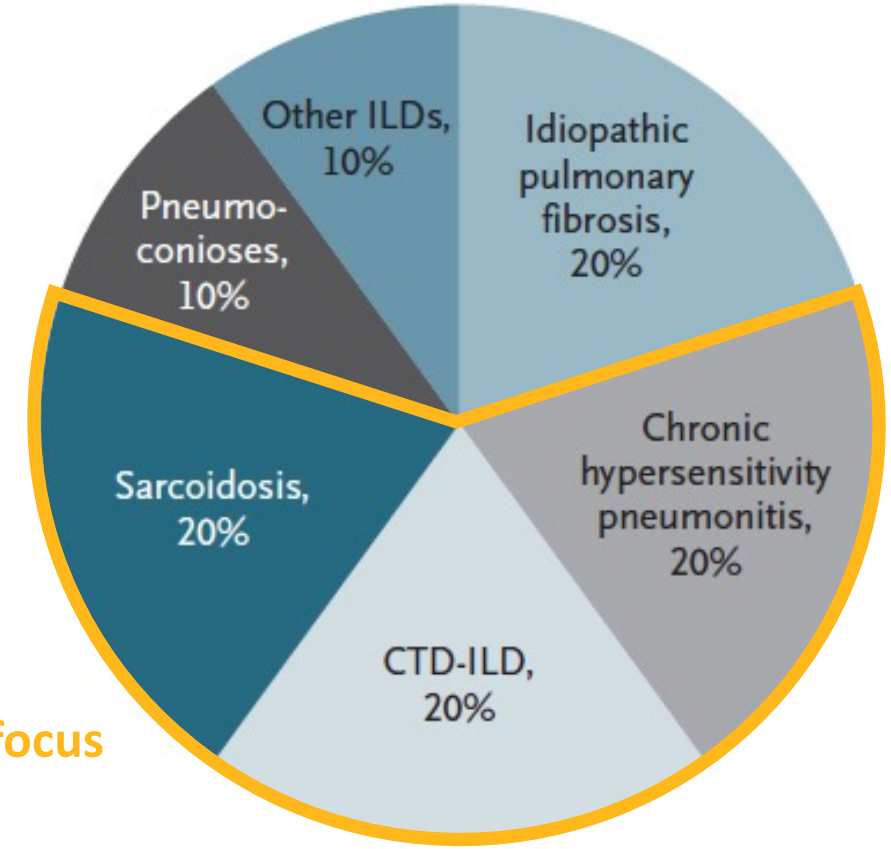


- ILDs lie on a spectrum of inflammation and fibrosis, but all share an immune pathology
- Progression to fibrosis is a key driver of morbidity and mortality
- By targeting aberrant immune response driving fibrosis, ATYR1923 has potential to improve outcomes in multiple ILDs

Slide adapted from Dr. Steven Nathan, Medical Director, Advanced Lung Disease and Transplant Program at Inova Fairfax Hospital, Falls Church, VA

Market Opportunity in Inflammatory Interstitial Lung Disease

Relative Distribution of ILDs in the USA(1)



- >200 types of ILD: 4 major types comprise 80% of patients
- Limited standard of care with substantial morbidity and mortality
- aTyr focused on 3 most inflammatory types: ~500-600k US patients(2); ~3m globally
- $2-3b global market opportunity(3)

(1) Lederer, Martinez. NEJM 2018
(2) All ILDs individually have potential for orphan status
(3) aTyr estimates for ATYR1923 in Pulmonary Sarcoidosis, CHP, CTD-ILD; excludes IPF

First ATYR1923 Indication: Pulmonary Sarcoidosis

- Inflammatory disease of unknown etiology characterized by the formation of granulomas (clumps of immune cells)
- T cell driven: CD4+ (Th1 / Th17)
- Pulmonary sarcoidosis occurs in ~90% of all sarcoidosis patients
- Treatment options are limited with associated toxicity: Corticosteroids, antimetabolite immunosuppressants, TNF inhibitors

50% require systemic therapy

30% have chronic progressive disease despite available treatment

Culver et al. BMJ 2019; Baughman ATS Annals 2016

ATYR1923

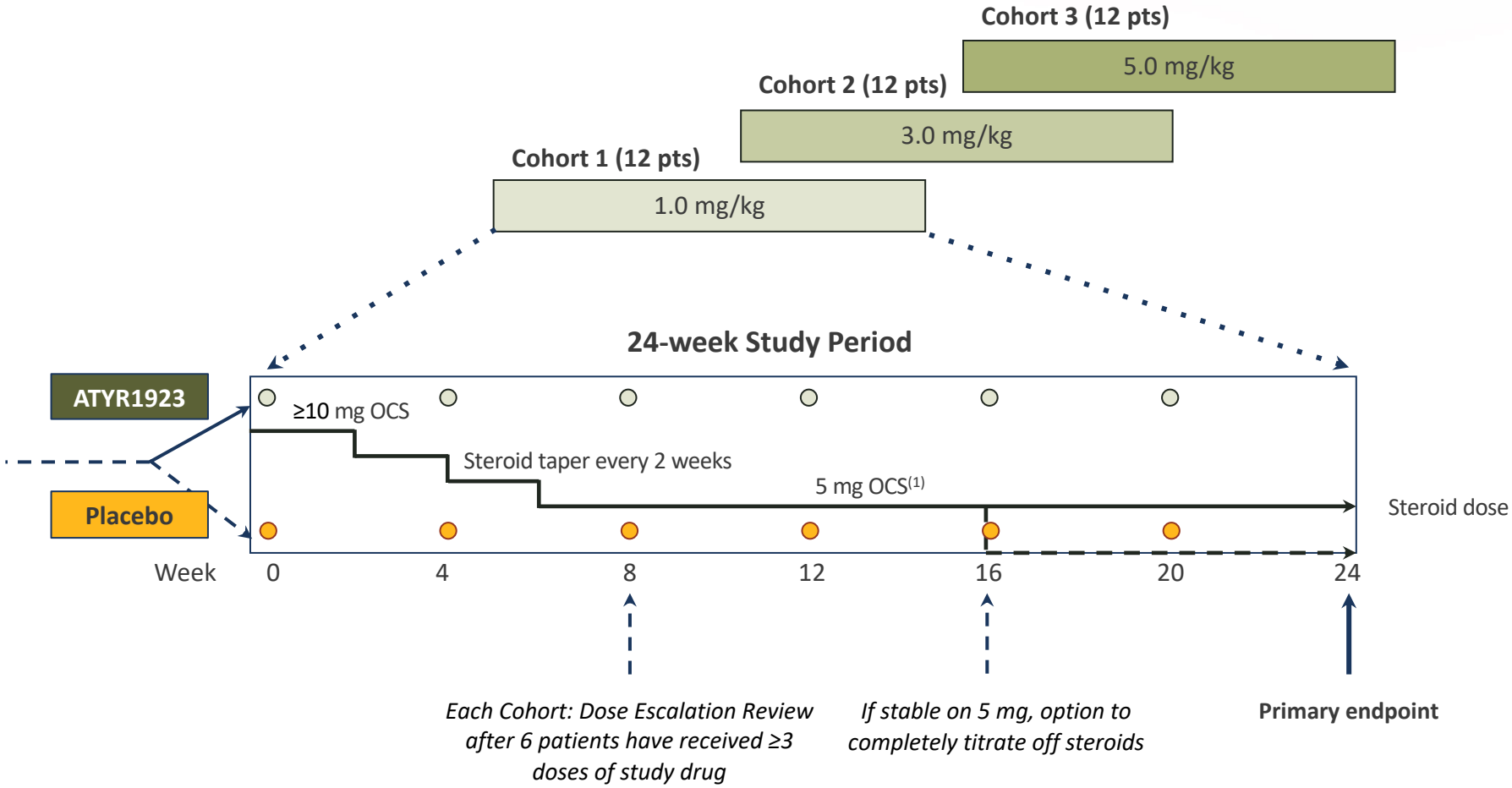
Phase 1b/2a Study in Pulmonary Sarcoidosis

Phase 1b/2a Study in Pulmonary Sarcoidosis Ongoing

Design	• Randomized (2:1), double-blind, placebo-controlled, multiple ascending dose • 6 IV doses of ATYR1923 being tested at 1.0, 3.0, and 5.0 mg/kg • Forced steroid taper to 5.0 mg by week 8; taper to 0 mg possible at week 16 in responders
Population	• 37 histologically confirmed pulmonary sarcoidosis patients • ≥10 mg stable oral corticosteroid treatment • Symptomatic/active disease at baseline
Primary Endpoint	• Safety and tolerability of multiple ascending IV ATYR1923 doses
Secondary Endpoints	• Steroid-sparing effect • Immunogenicity • Pharmacokinetics (PK) • Exploratory efficacy measures: FDG-PET/CT imaging; Lung function (FVC); Serum biomarkers; Health-related quality of life scales

Enrollment completed. Data expected Q3 2021

Phase 1b/2a Pulmonary Sarcoidosis Study Schema

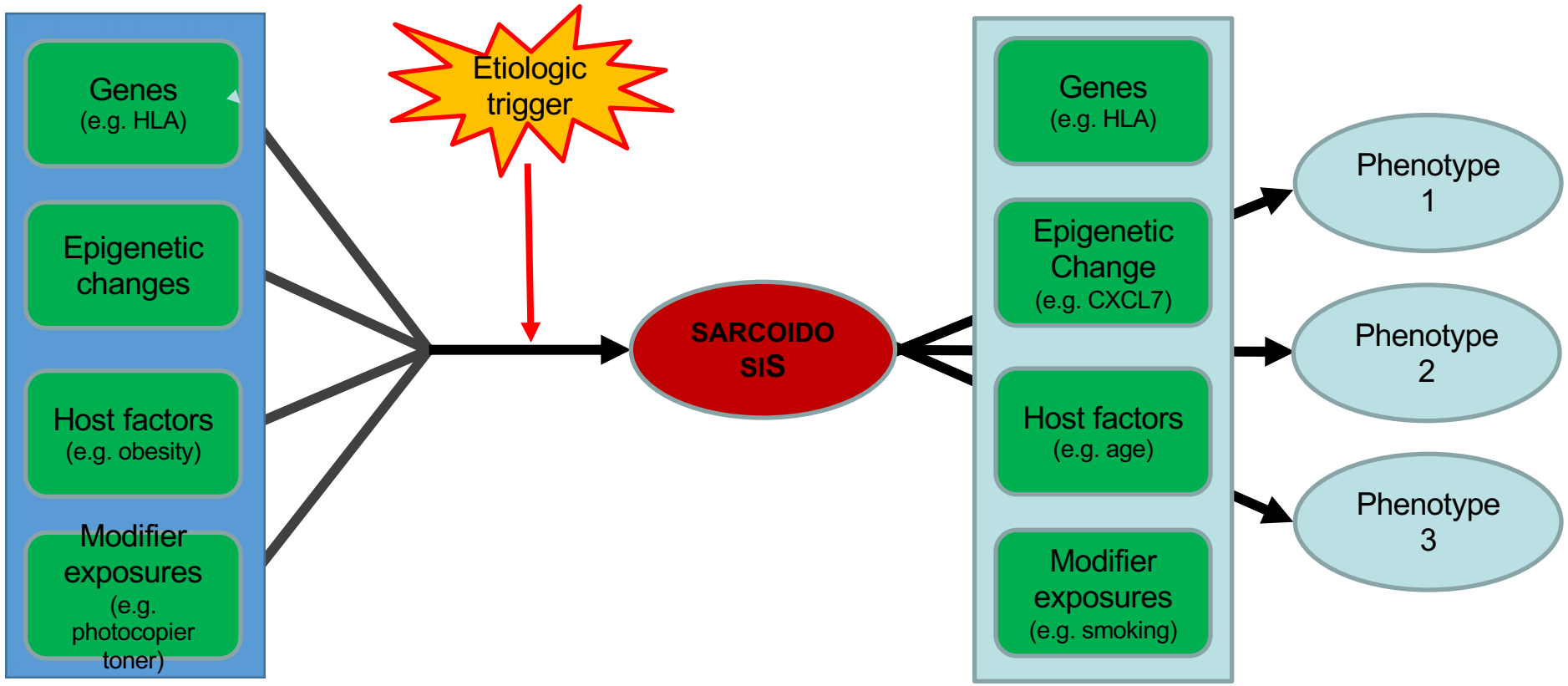


(1) subtherapeutic dose

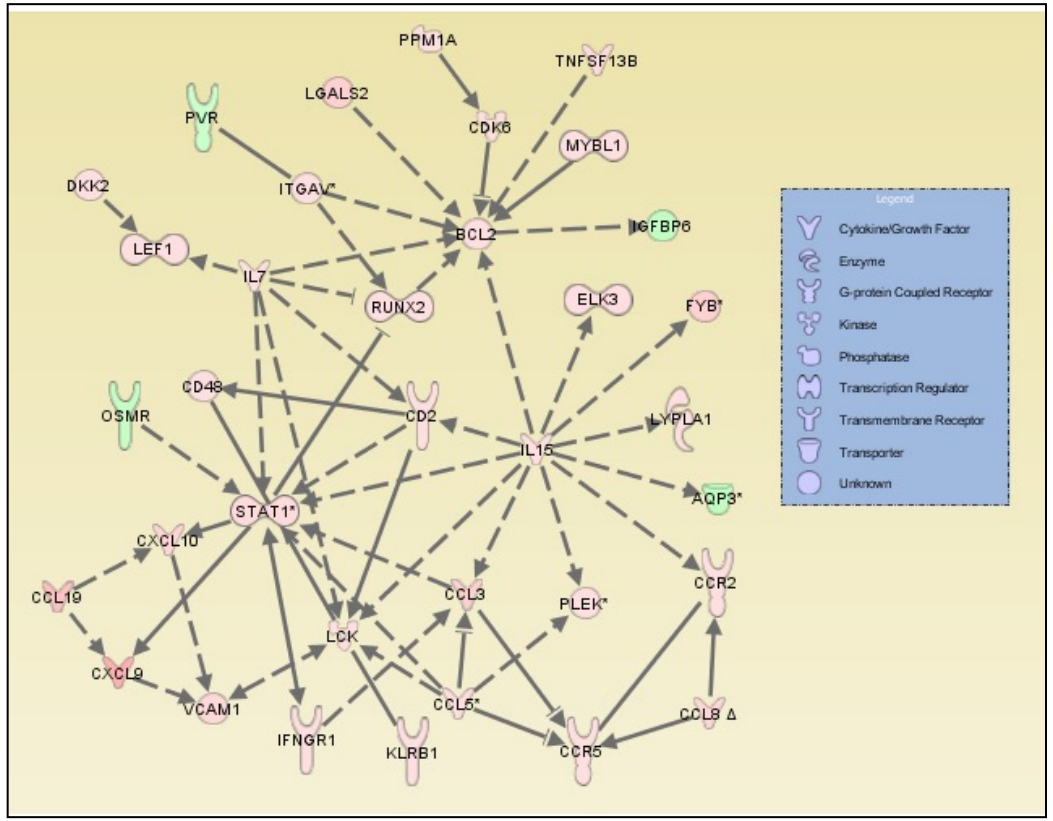
Sarcoidosis

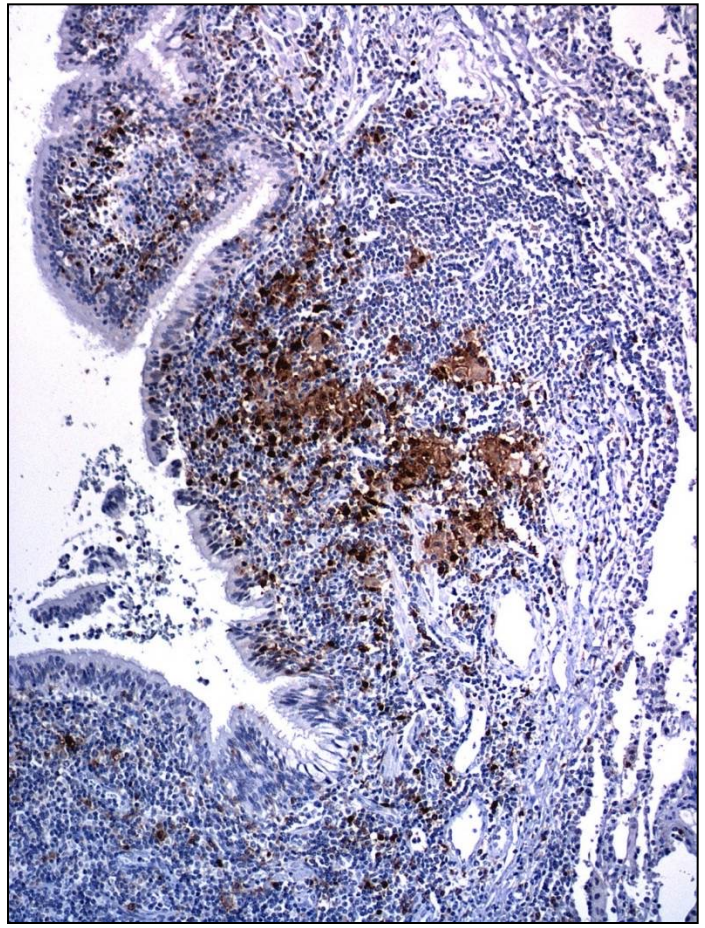
Daniel A. Culver, D.O.
Chair, Department of Pulmonary Medicine
Director, Diffuse Parenchymal Lung Disease
Cleveland Clinic

What causes sarcoidosis?

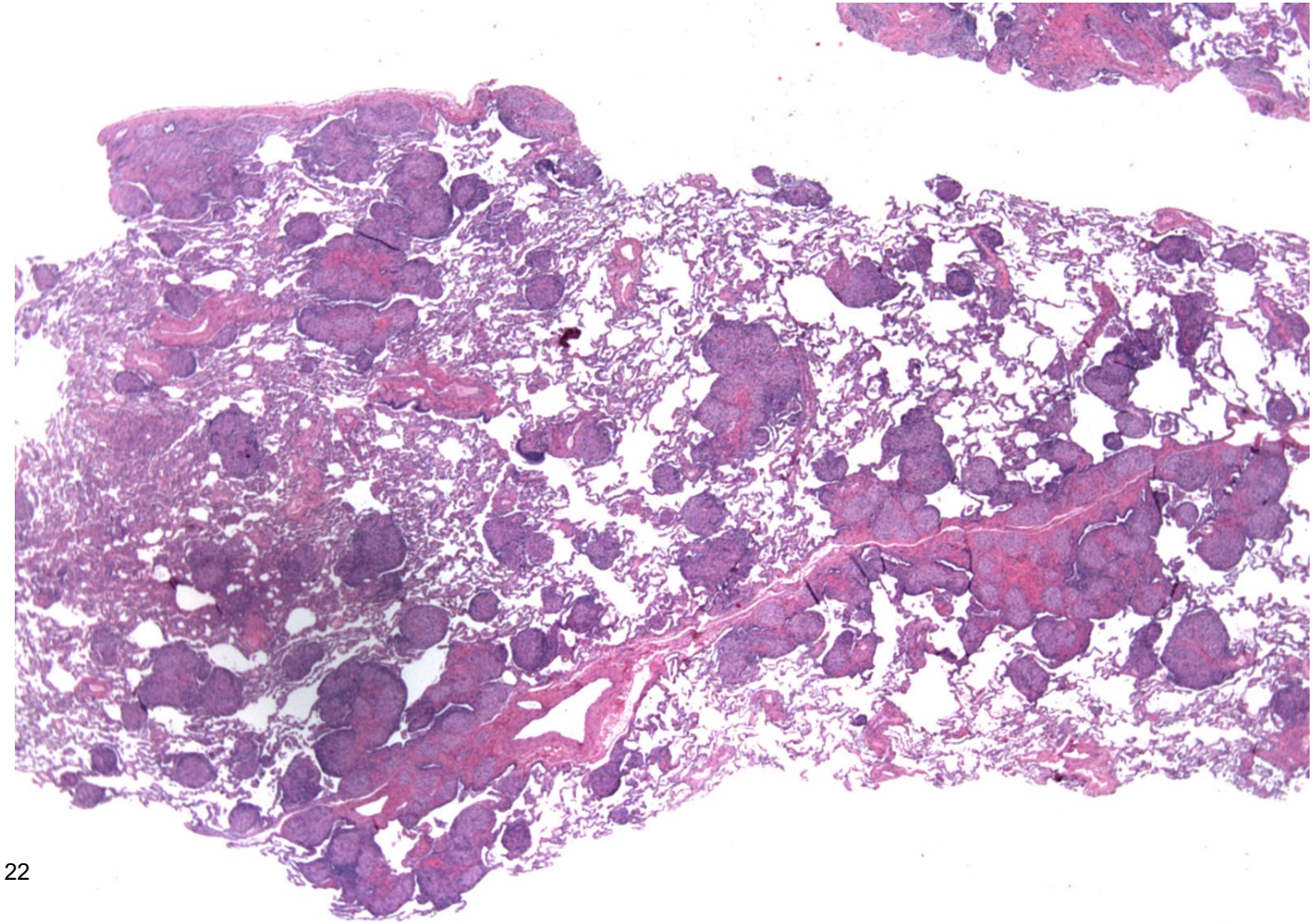


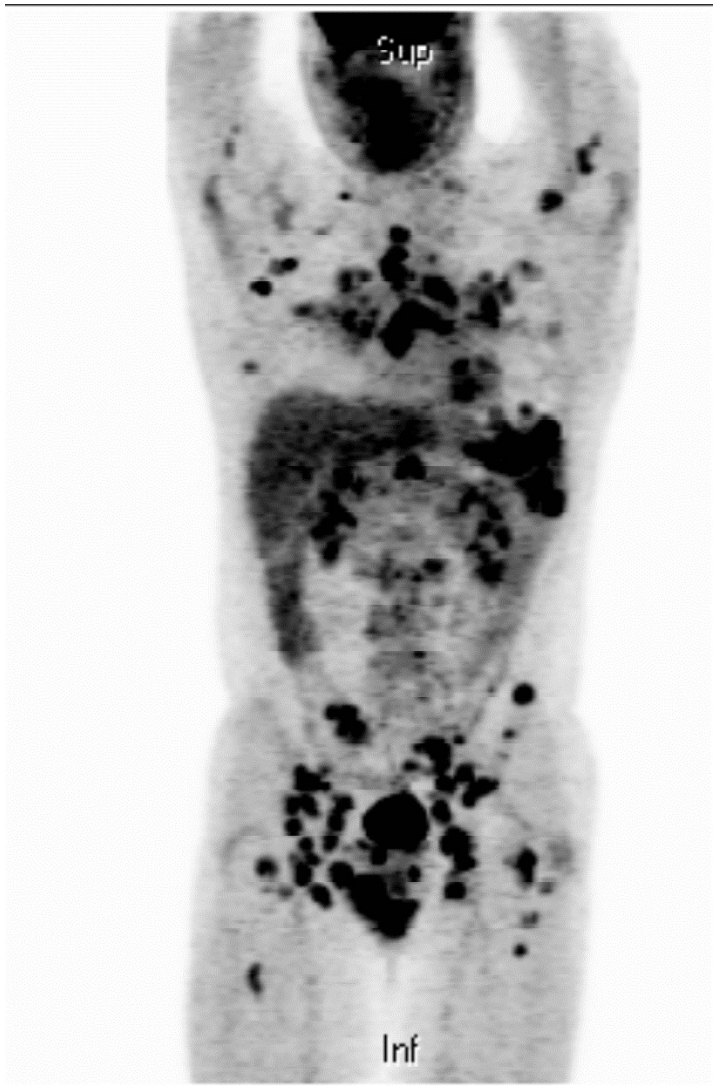
STAT1 plays a central role in sarcoidosis



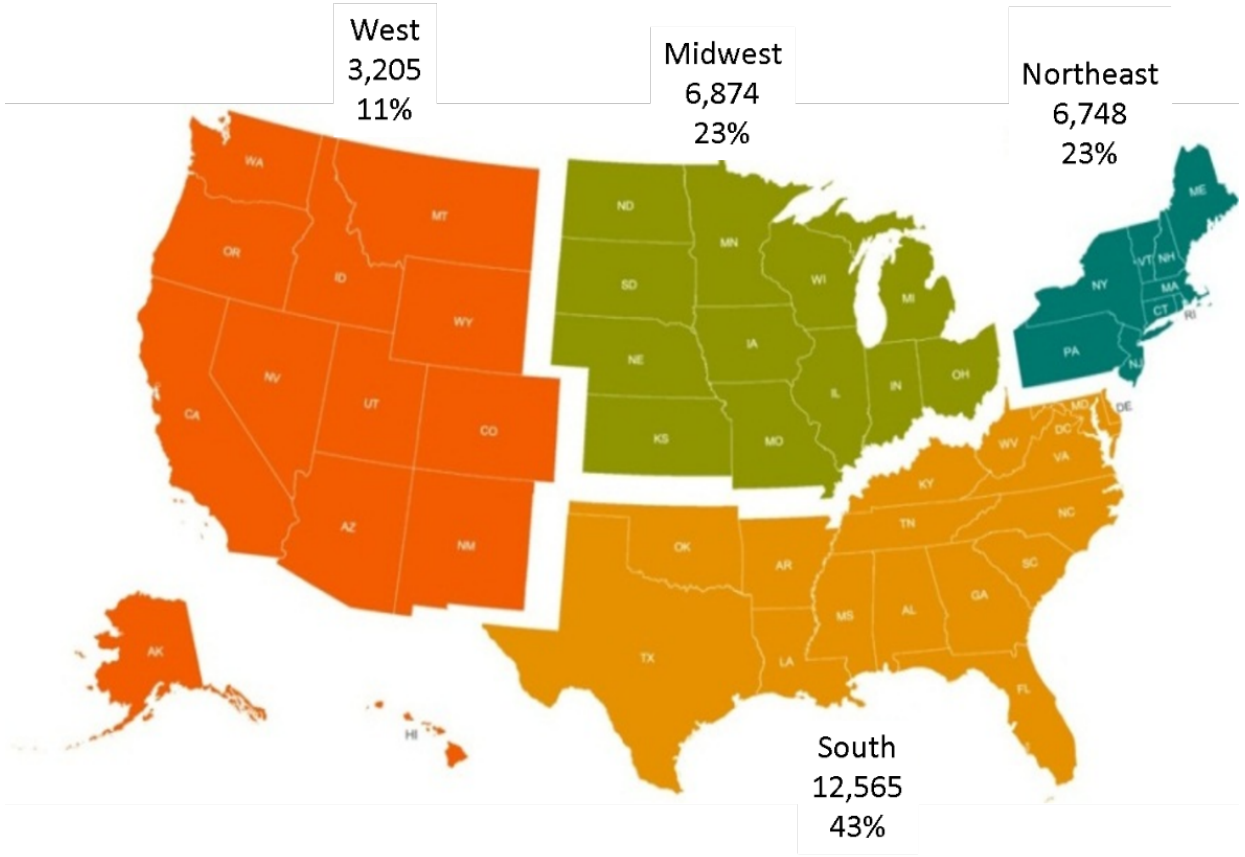


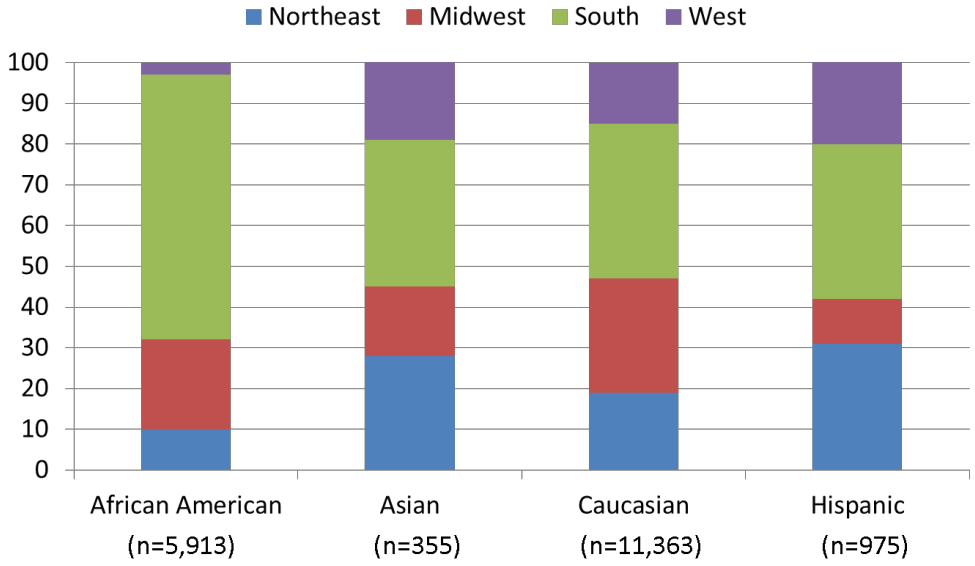
Sarcoidosis is a systemic granulomatous disease





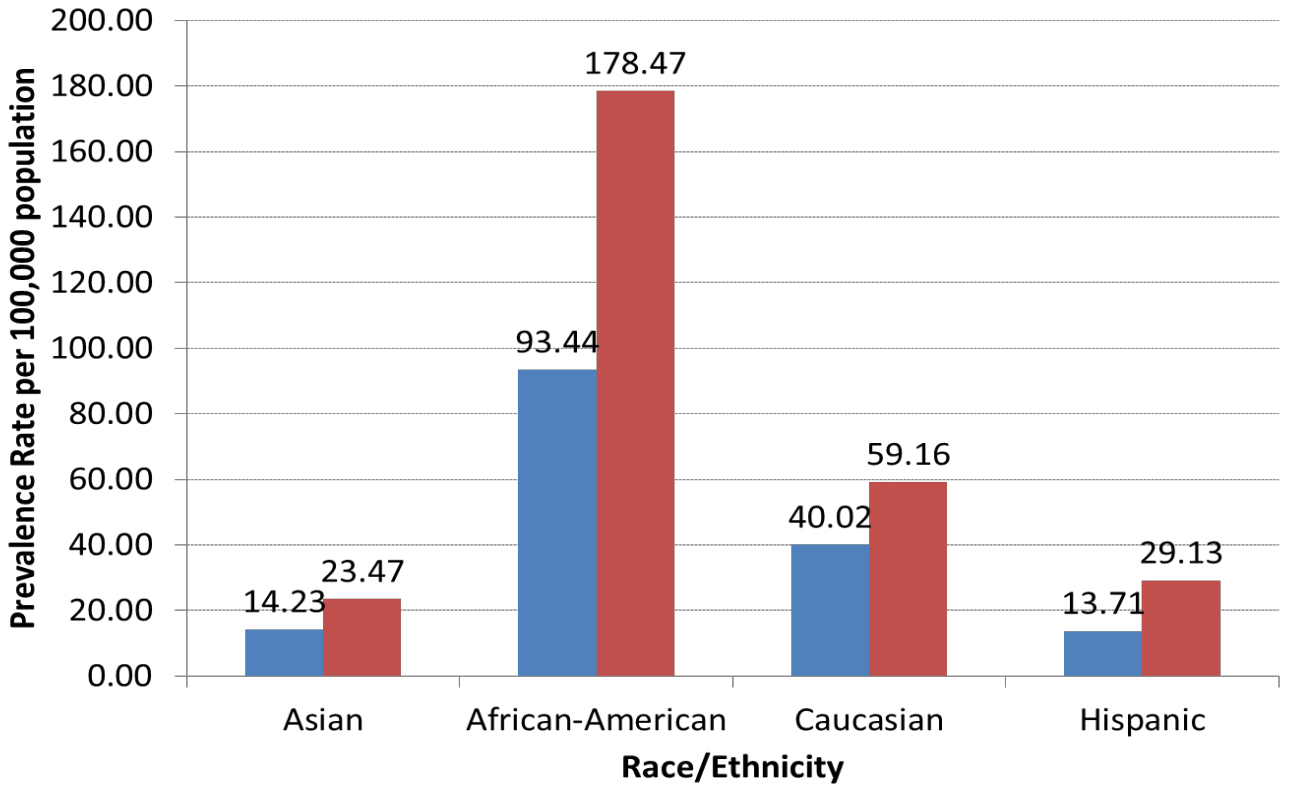
Sarcoidosis less common in the West





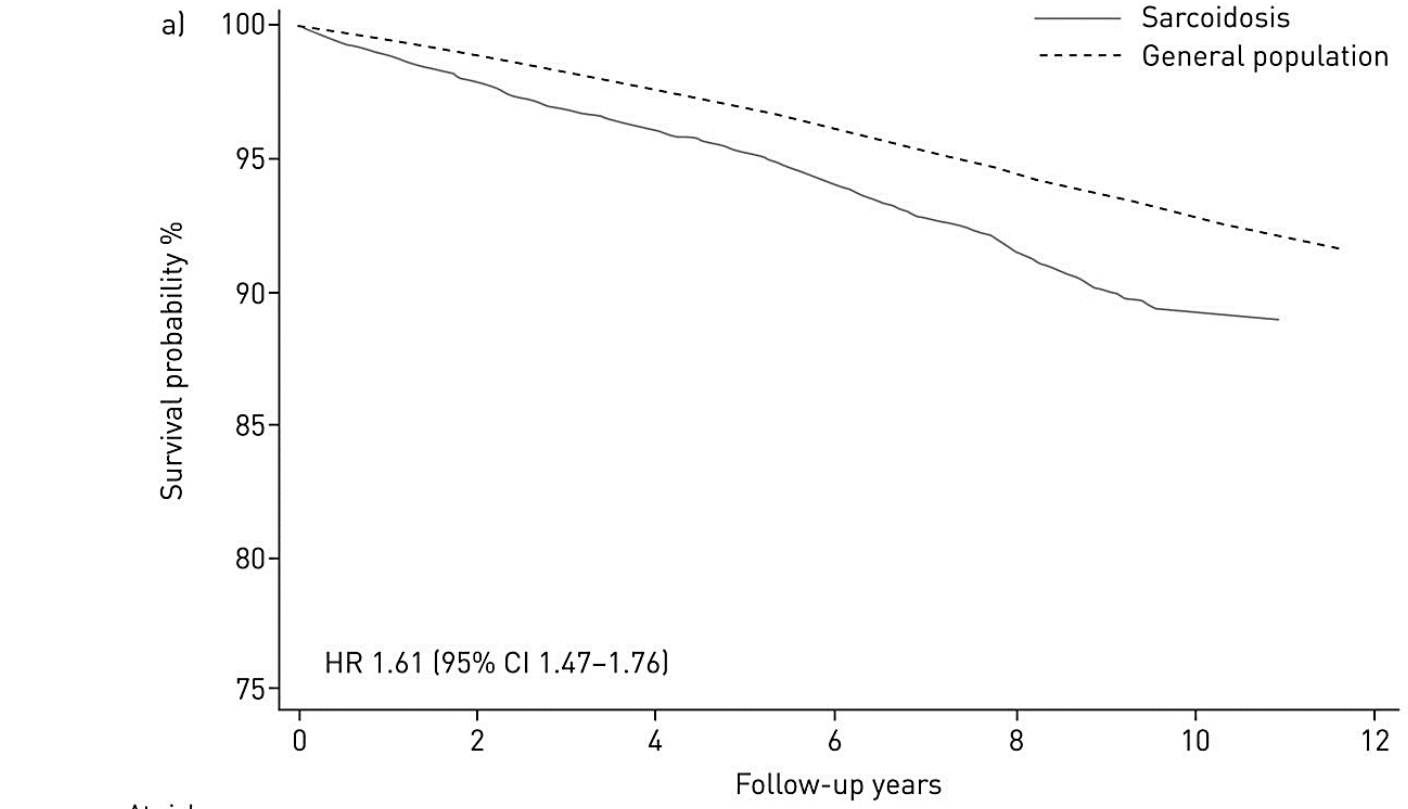
Baughman RP. Ann Am Thorac Soc 2016

Female predilection



Baughman RP. Ann Am Thorac Soc 2016

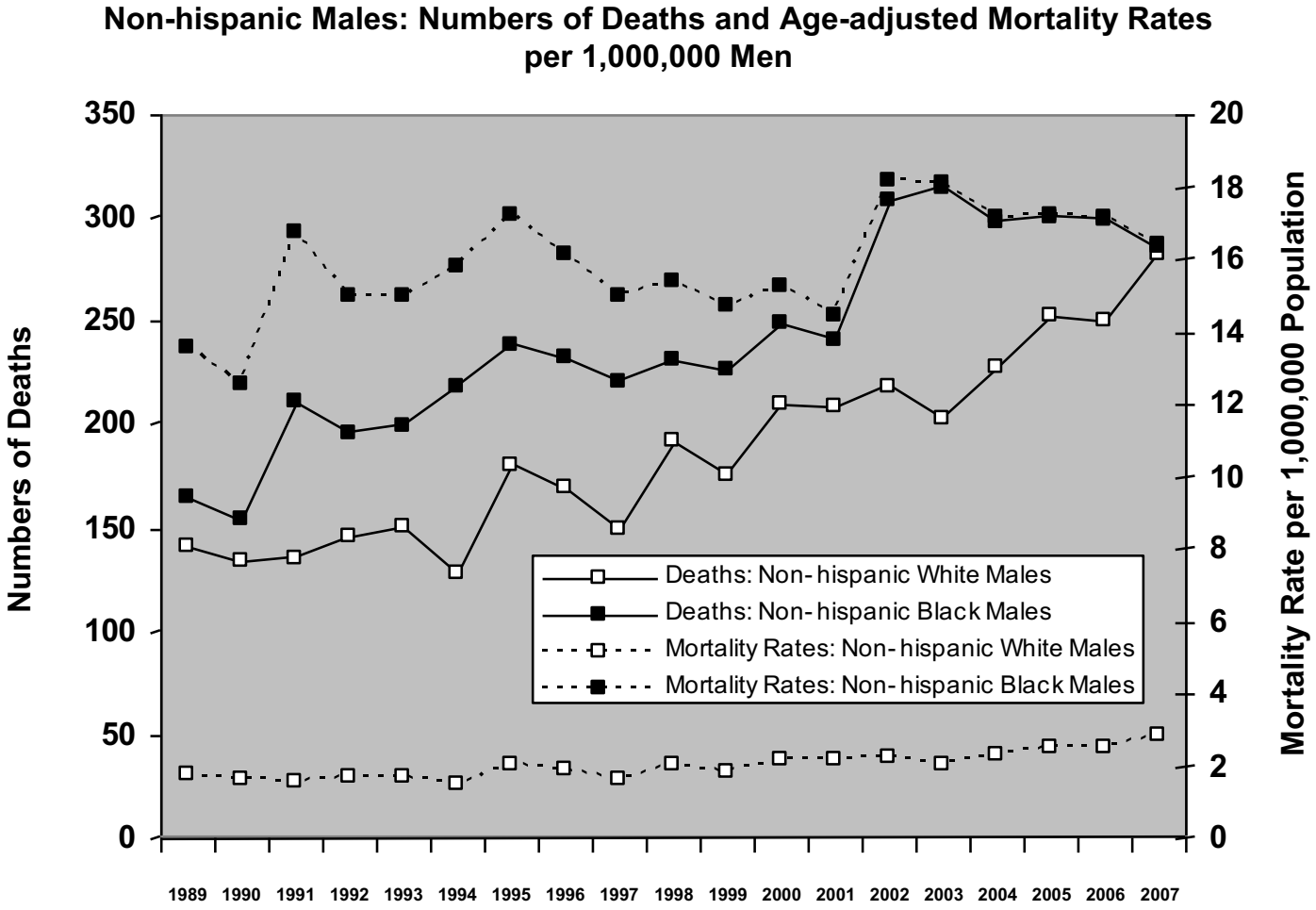
Mortality in Swedish sarcoidosis patients vs general population



At risk n							
Sarcoidosis	8207	7149	5431	3793	2337	1008	0
General population	81 119	71 368	54 516	38 252	23 614	10 227	0

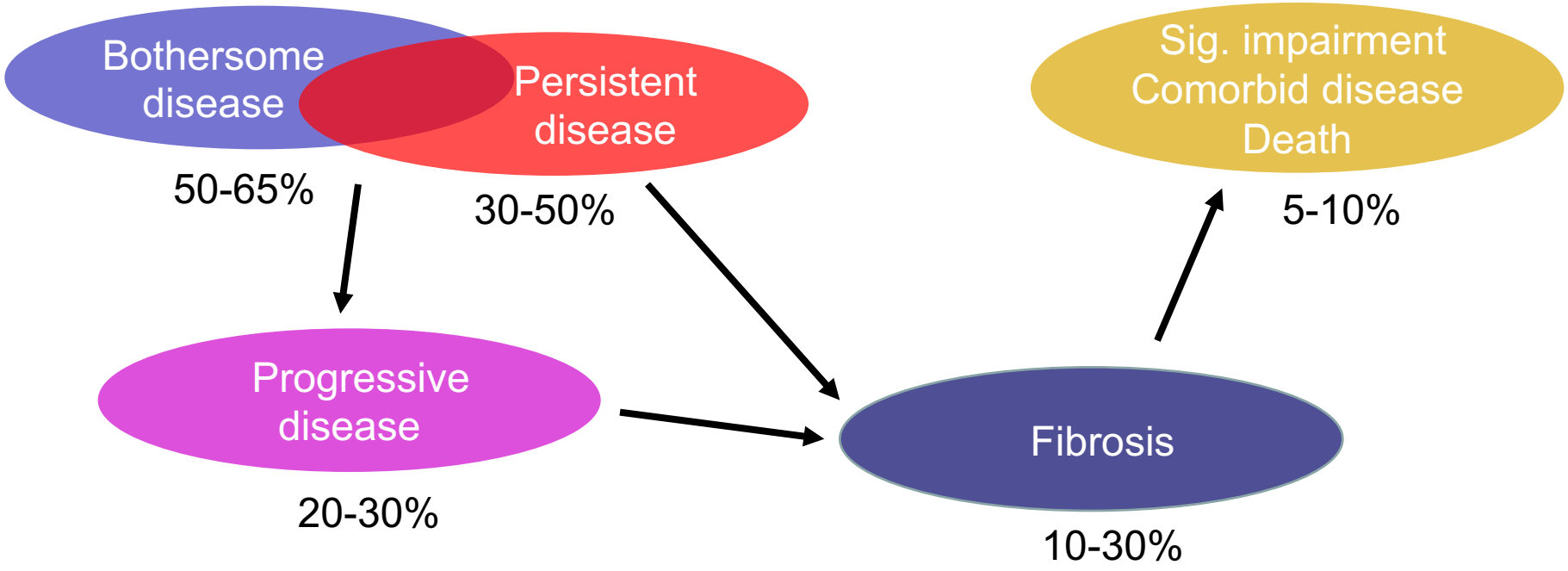
Rossides M. Eur Respir J 2018

Rising sarcoidosis mortality in the US



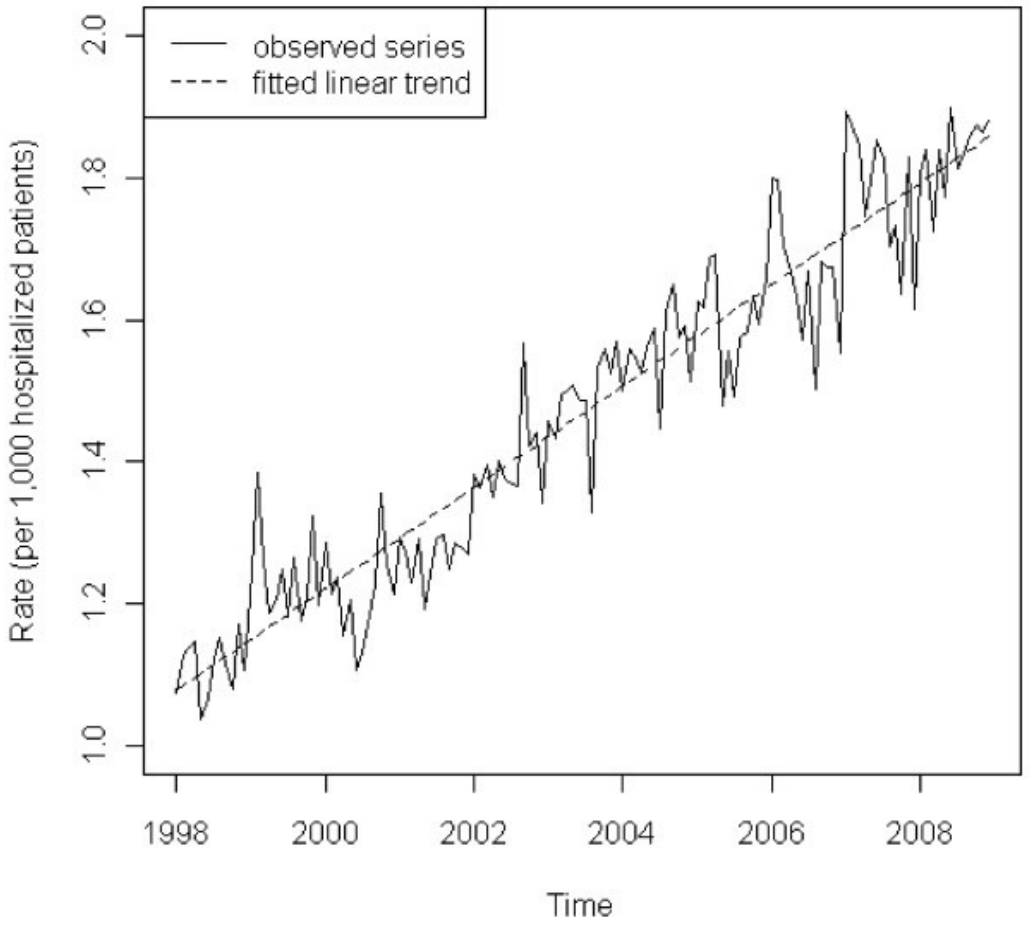
Swigris JJ. AJRCCM 2011

Which patient is at risk?



Baughman RP. QJM 2006; Mana J. Respiration 1994; Viskum K. Eur Respir J 1993; Nagai S. Curr Opin Pulm Med 1999; Judson MA. SVDLD 1993; Neville E. QJM 1983; Israel HL. Ann NY Acad Sci 1986;

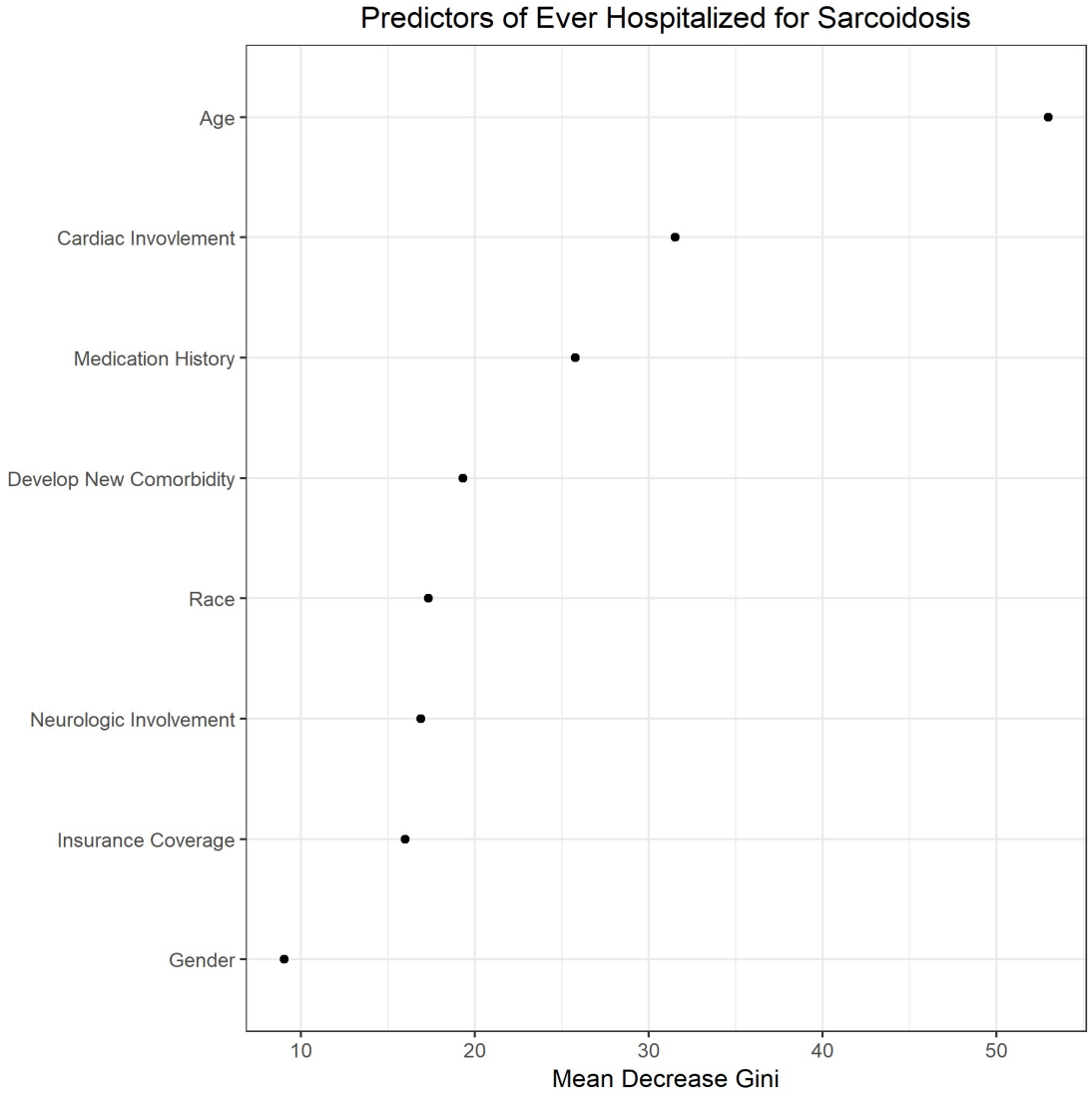
Hospitalizations are rising



Gerke AK. BMC Pulm Med 2012

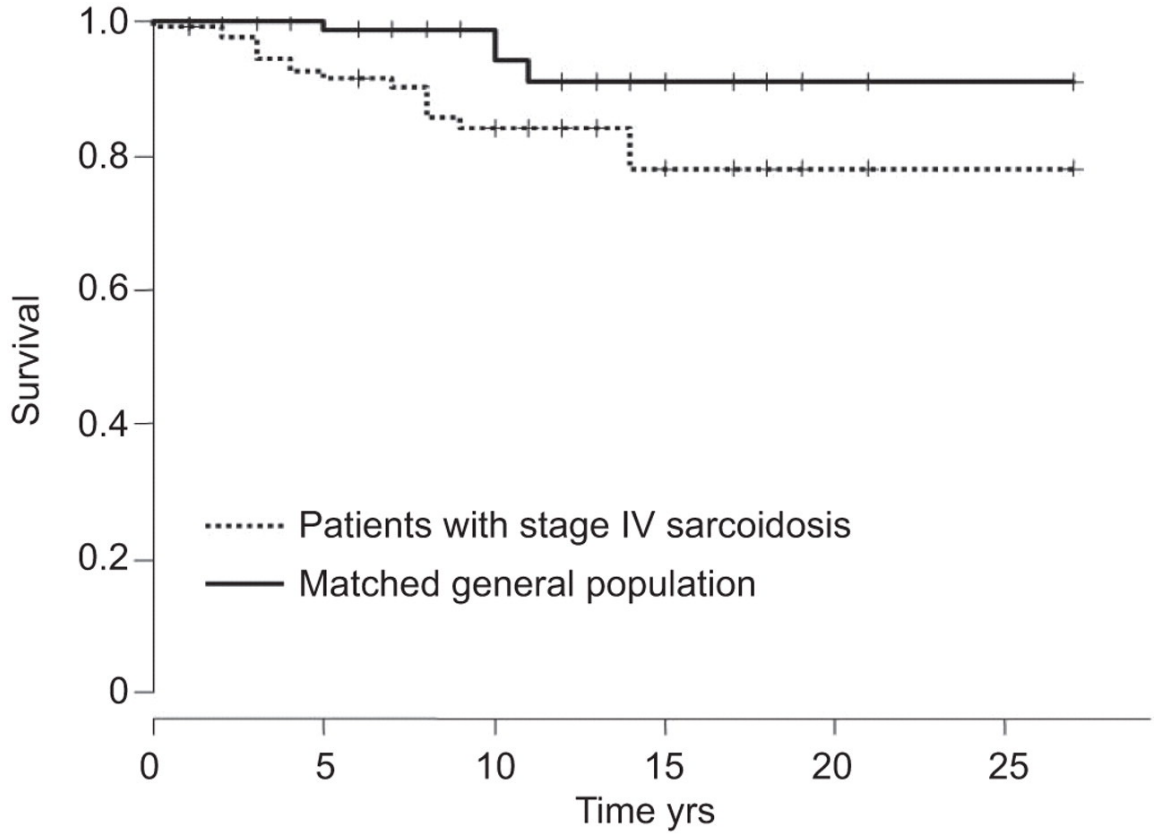
Ever hospitalized for sarcoidosis?

Variable	Odds ratio
Age/yr	0.99 (0.98-0.99)
Male gender	1.4 (1.1-1.9)
Race White Black Other	 Ref 1.7 (1.1-2.3) 1.0 (0.6-1.5)
Insurance Private Government None	 Ref 1.6 (1.2-2.1) 2.1 (0.99-4.5)
Neurologic	2.1 (1.6-2.8)
Cardiac	4.9 (3.3-7.3)
Sarcoidosis medications Never Past Current	 Ref 1.7 (0.96-3.0 3.1 (1.9-5.0)
Comorbidity	2.1 (1.6-2.7)



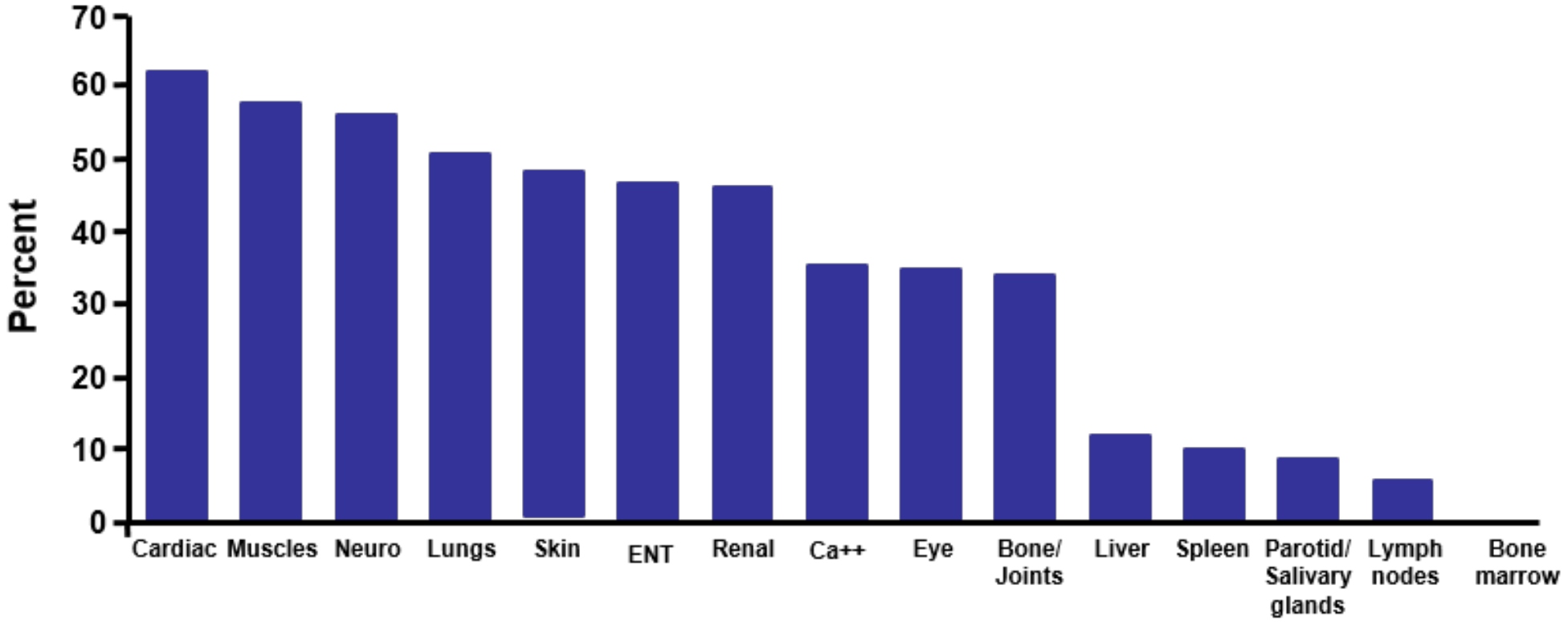
Fibrotic sarcoidosis impact on survival

Comparison of survival between patients with radiographic stage IV disease and a matched French general population (n=142).



Nardi A. Eur Respir J 2011

Frequency of treatment requirement



Judson MA. Sarcoidosis Vasc Diffuse Lung Dis 2012

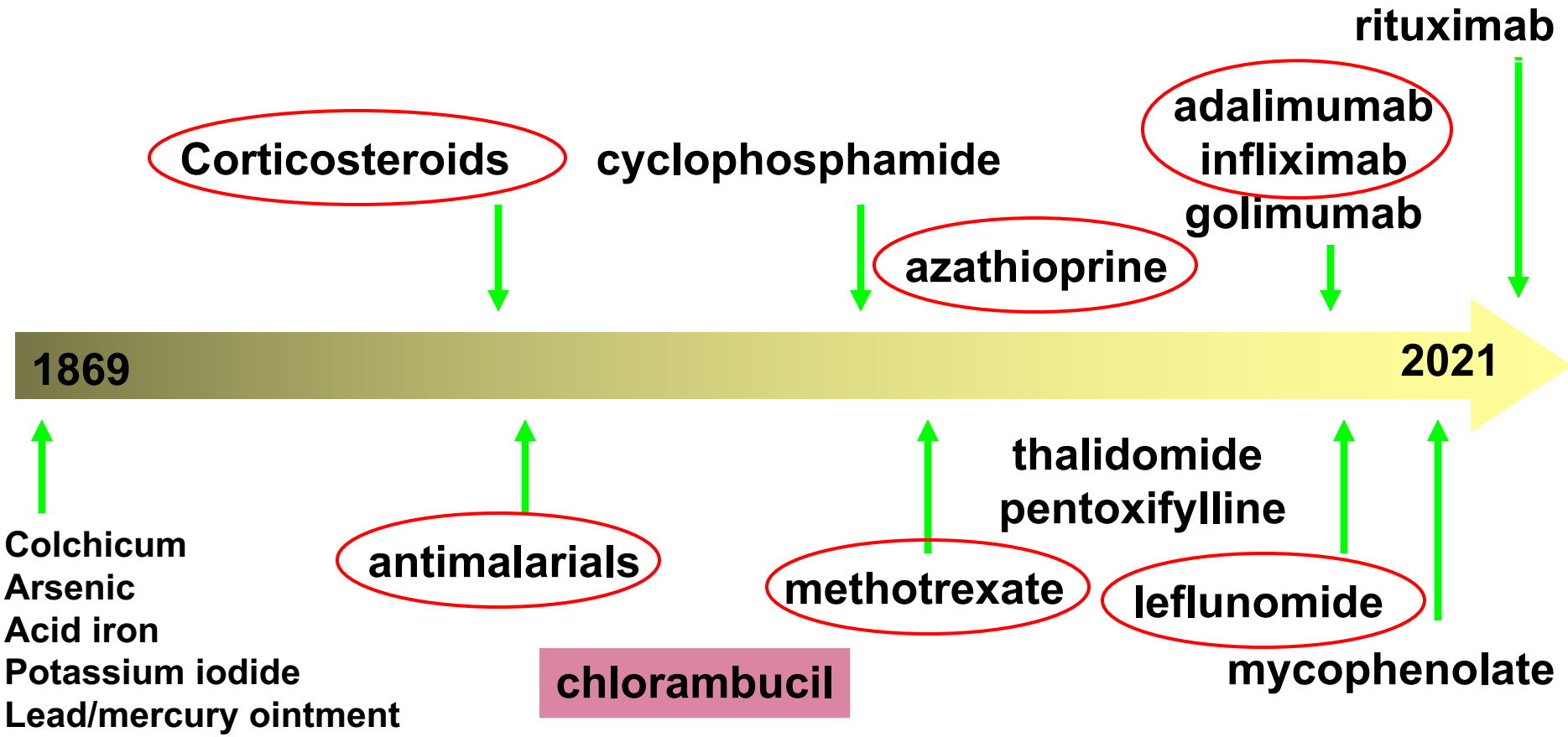
Prognostic markers

Increasing number of organs versus outcome

Outcome at 2-5 yrs	1 organ (n=44)	2-3 organs (n=198)	4+ organs (n=53)
No important issue	64%	46%	13%
Significant organ function impairment	30%	43%	64%
Required assistance	7%	6%	23%

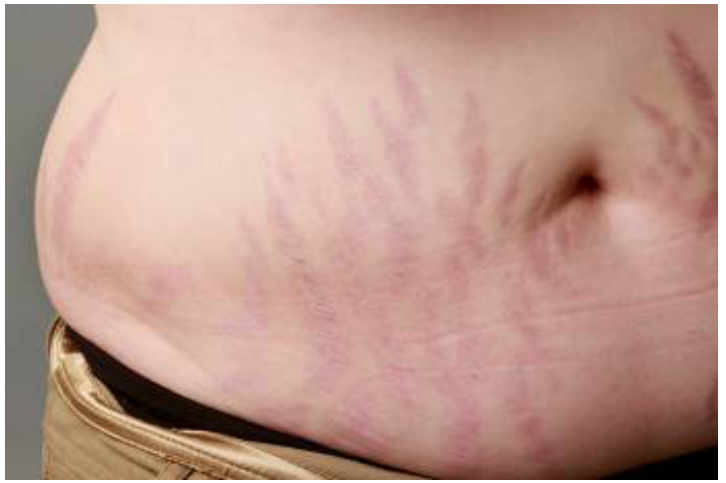
Takada K. J Clin Epidemiol 1993

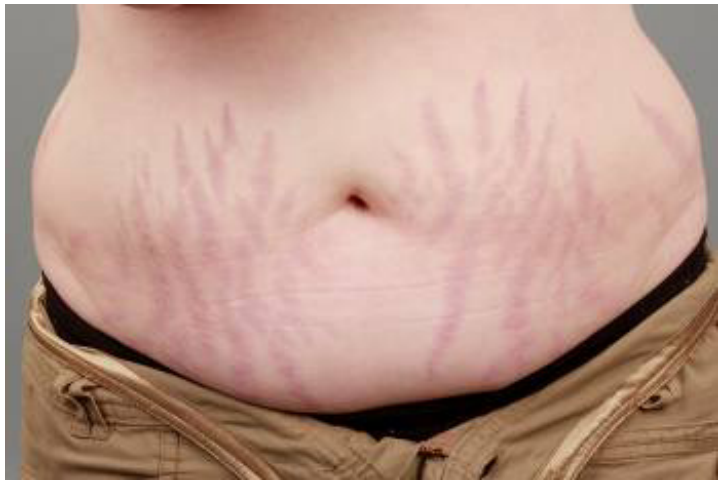
Main immunosuppressive options



Glucocorticosteroids

- Glucocorticosteroids
  - first-line treatment in systemic sarcoidosis
  - most commonly used
- Alternative second-line agents important
  - steroid-resistance
  - steroid-induced side-effects
  - steroid-sparing

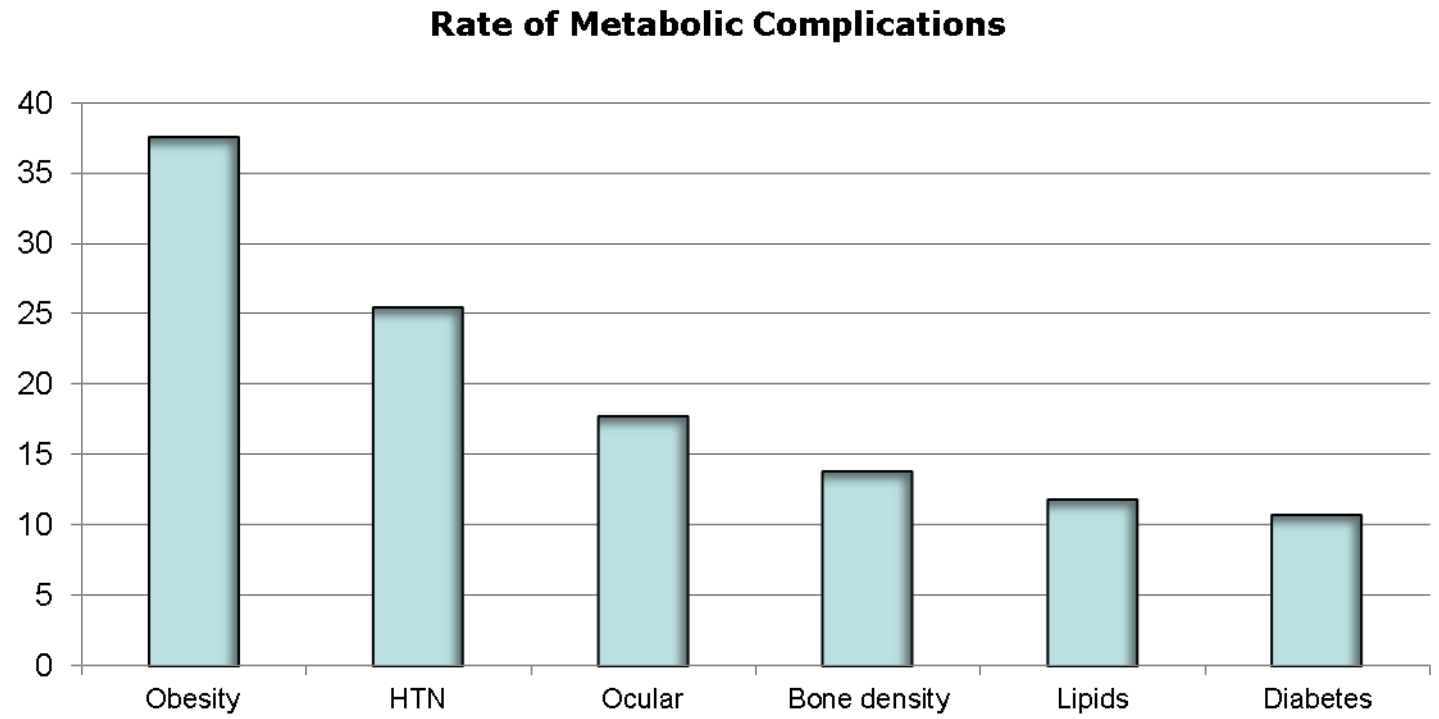




Metabolic Complications among 154 new sarcoidosis patients seen at CCF

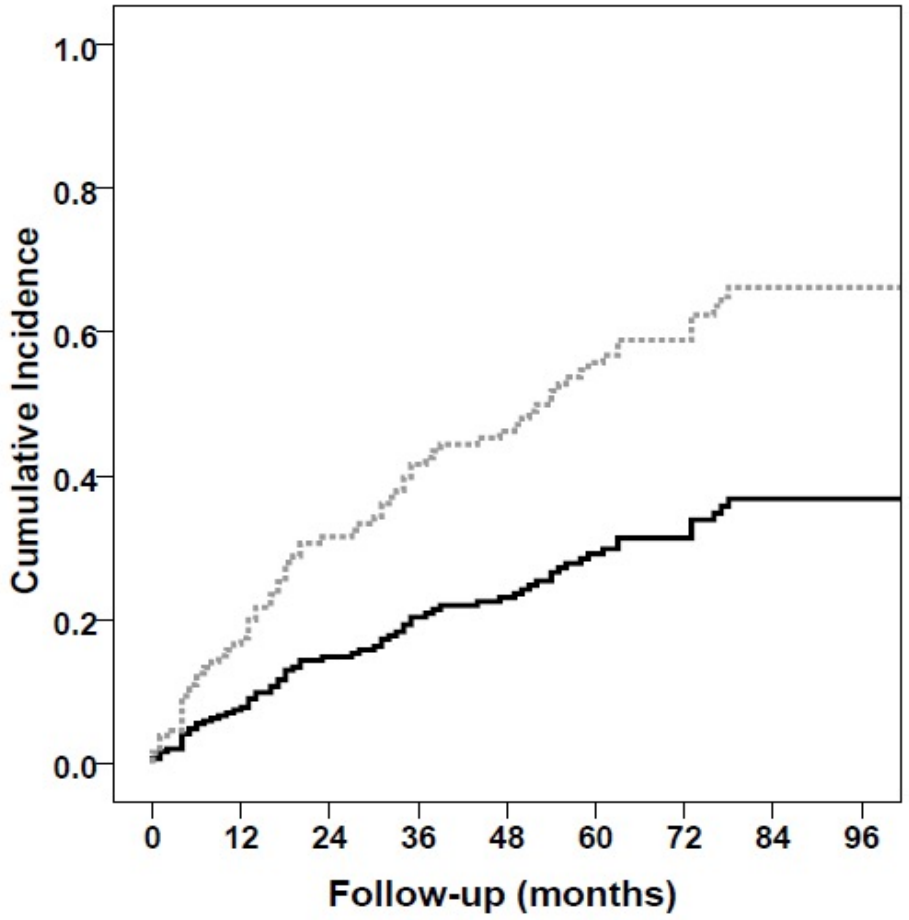
76 patients developed or had worsening

average of 1.9 ± 1 conditions per patient



Khan N. Resp Med 2017

Cumulative risk of steroid complications among newly diagnosed individuals at Cleveland Clinic



Hazard ratio: 2.37 (1.34-4.17)

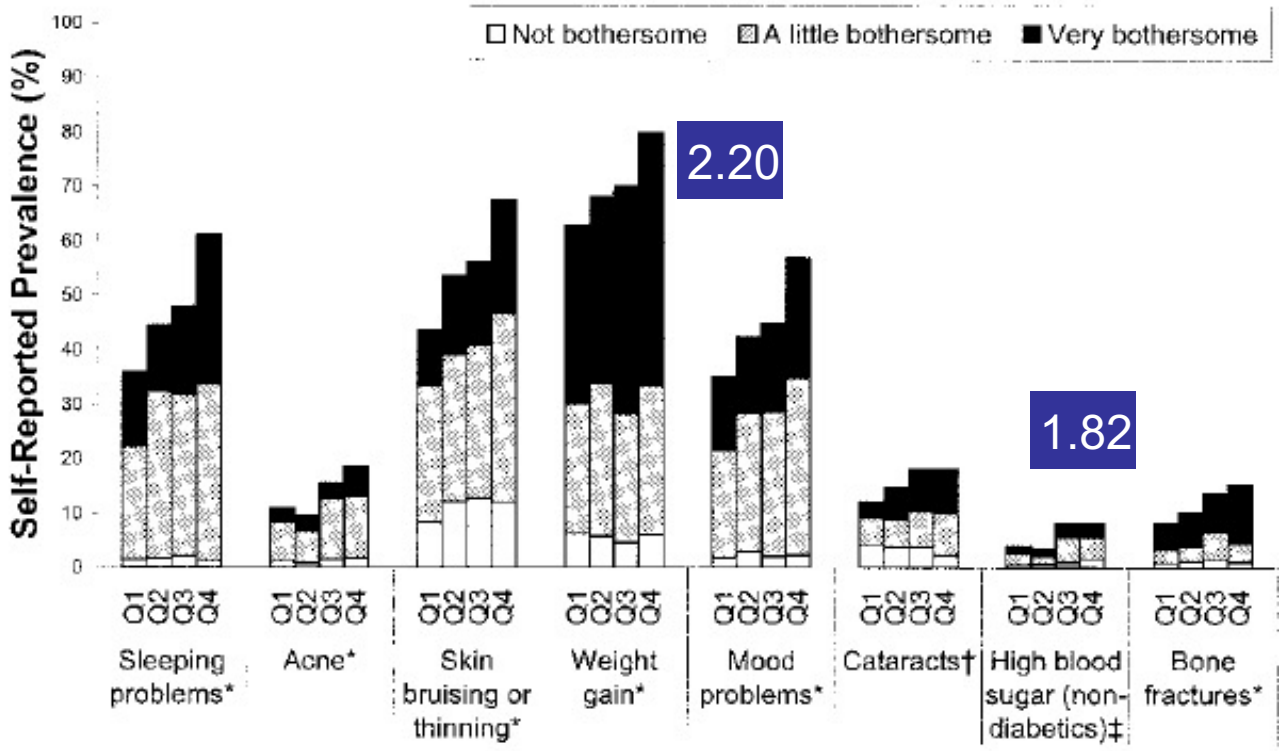
Other covariates

Age/yr	1.021	(1.001-1.041)
Pre-existing disease	2.27	(1.33-3.89)
Duration of steroids (mos)	1.023	(1.013-1.033)
Cumulative dose (grams)	1.038	(1.019-1.056)

Khan NA. Respir Med 2017

Rate of eight complications in individuals using GC > 60 days

n=2167 patients



Curtis JR. Arthritis Rheum 2006

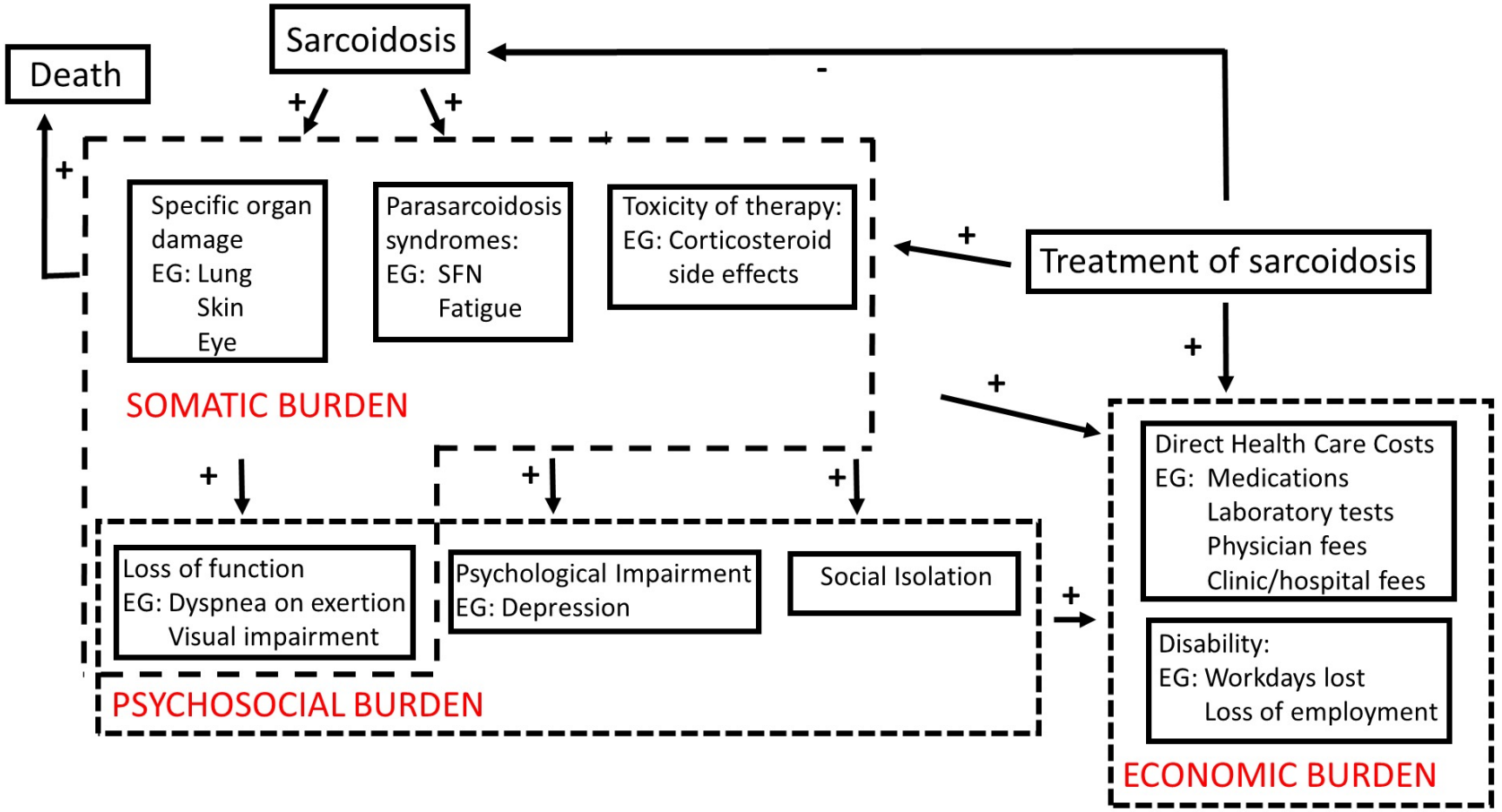
Steroids are associated with impaired QOL

Table 3—*Differences in Predicted HRQL Scores Between Patient Groups Based on Oral Corticosteroid Treatment**

Group	Unadjusted Score	p Value	Adjusted Score†	p Value	Adjusted Score‡	p Value
SGRQ total						
Steroid users (n = 56)	52 (45–58)	<0.0001	49 (43–56)§	0.031	48 (44–53)‖	0.011
No steroids (n = 55)	37 (31–43)		39 (33–44)		39 (35–44)	
SF36-PCS						
Steroid users (n = 56)	31 (28–34)	0.011	32 (29–35)¶	0.048	32 (29–35)#	0.044
No steroids (n = 55)	37 (34–40)		37 (34–40)		37 (34–40)	
SF36-MCS						
Steroid users (n = 56)	42 (39–46)	0.055				
No steroids (n = 55)	47 (44–50)					

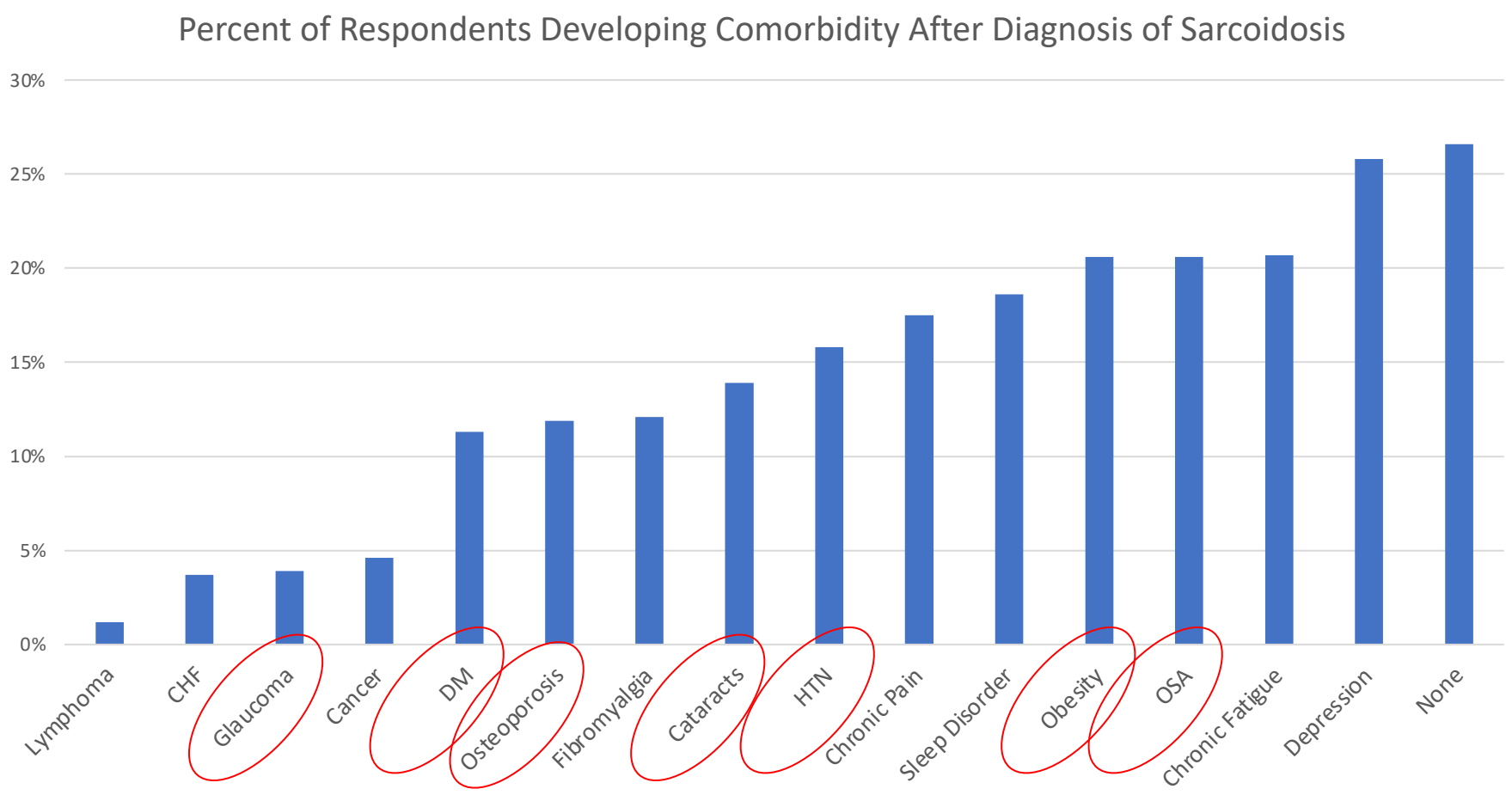
Cox CE. Chest 2004

Sarcoidosis burden



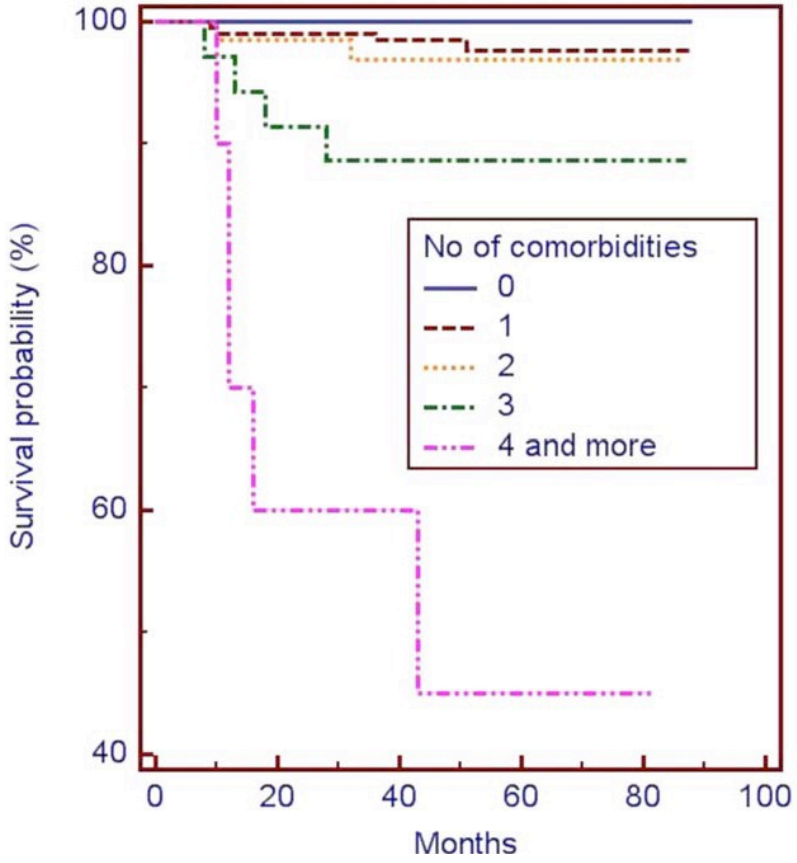
Gerke AK. Ann Am Thorac Soc 2017

Self-reported comorbidities in registry patients



Presence of comorbidities effect on survival

POLAND

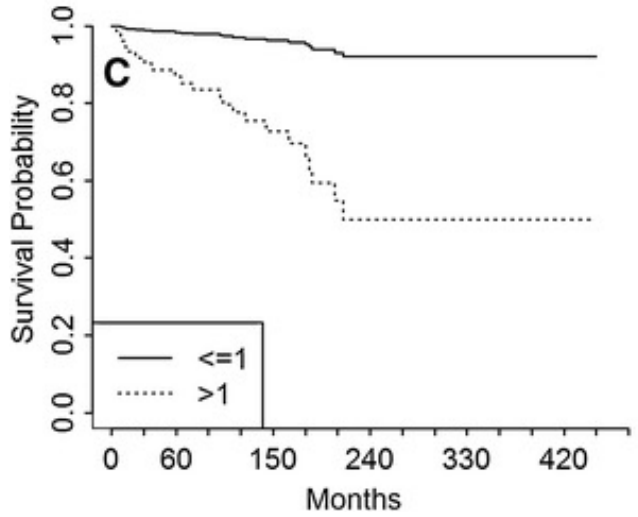


Nowinski A. Clin Respir J 2018

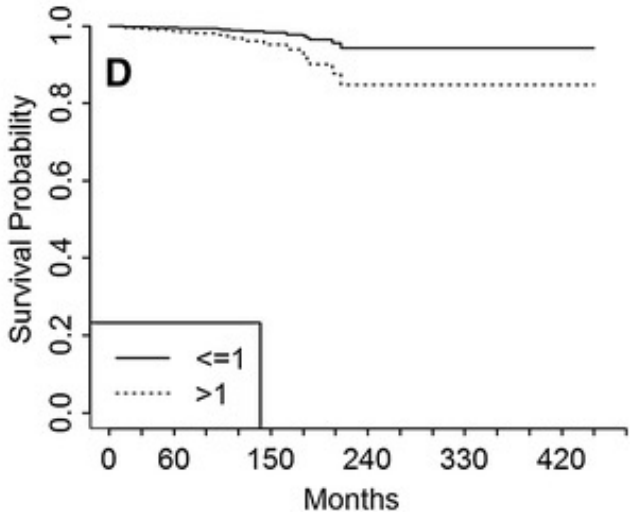
SPAIN

Charlson Comorbidity Index

Unadjusted



Adjusted



Brito-Zeron P. Lung 2018

A New Path to Medicine

aTyr: A New Path to Medicine

tRNA Synthetase Biology	• Platform of proprietary new biology
ATYR1923	• Novel MOA for inflammatory lung disease • Demonstrated effects in multiple animal lung injury models • Generally safe and well tolerated in previous Phase 1 and 2 studies • Proof-of-mechanism from biomarker data from Phase 2 study in COVID-19 • Phase 1b/2a results in pulmonary sarcoidosis patients expected Q3 2021
ATYR2810	• IND enabling activities for lead anti-NRP2 antibody in cancer
Discovery	• Potential new pipeline opportunities for additional NRP2 antibodies • Identification of new receptor targets for AARS and DARS
Capitalization	• Sufficient cash through next two primary catalysts • Supported by top tier investors including Federated and Fidelity

Thank You