ILD Collaborative

Project ECHO

Overview of Autoimmune ILD

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Why?

Common in new ILD

May have better survival

May benefit from anti-inflammatory

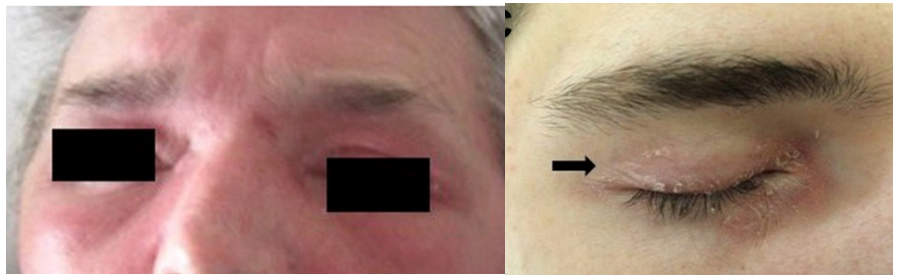
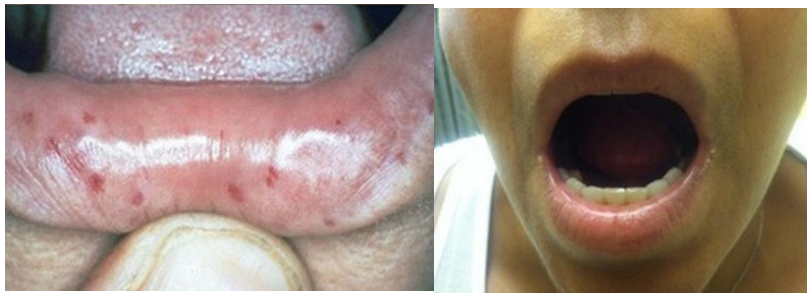
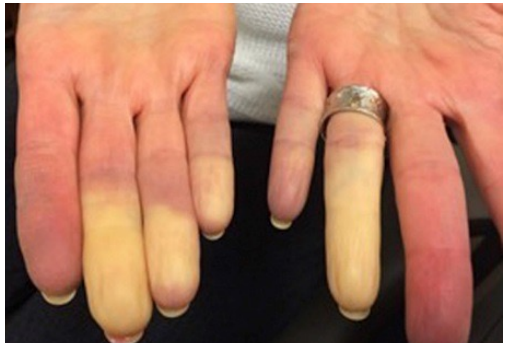
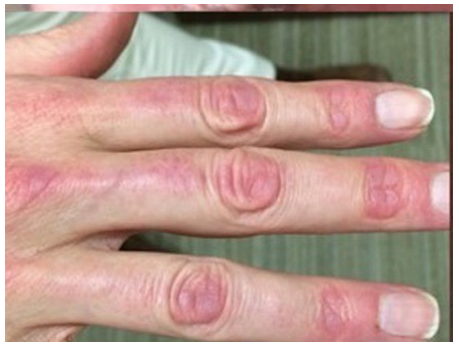
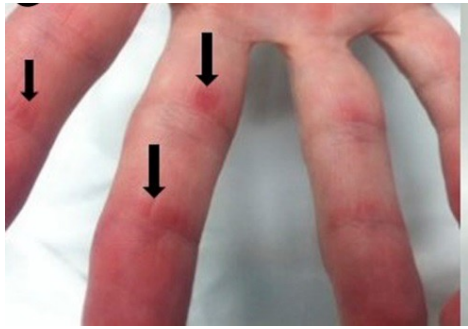
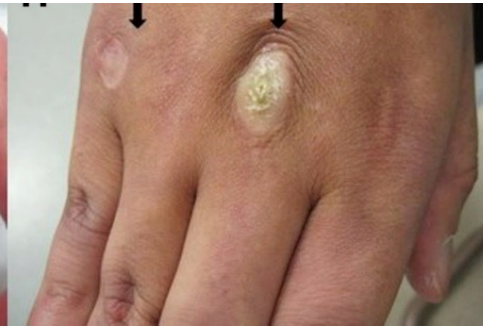
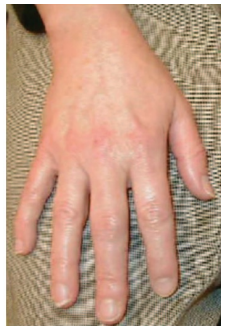
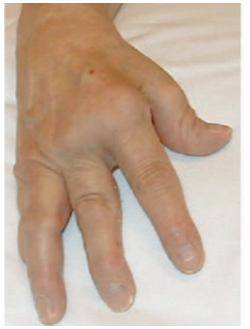
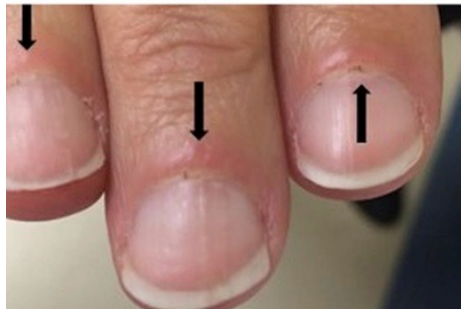
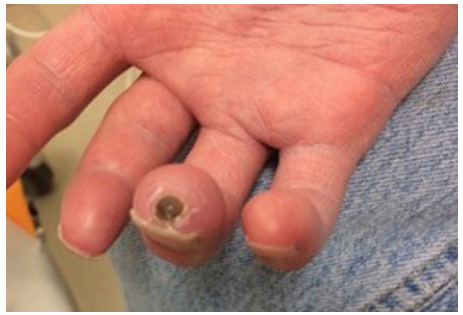
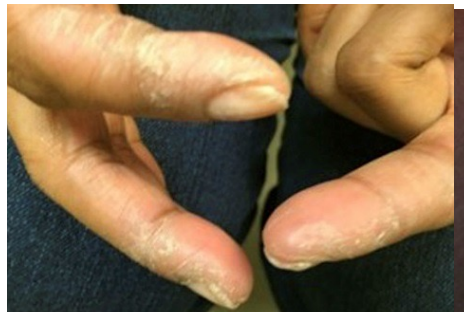
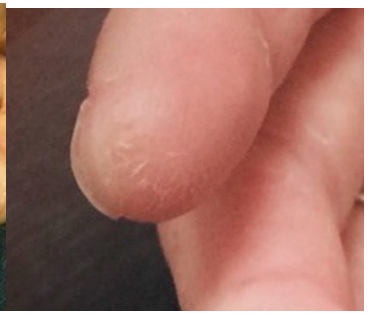
Systemic symptoms may need therapy

Find distinct pathogenesis and treatments

History

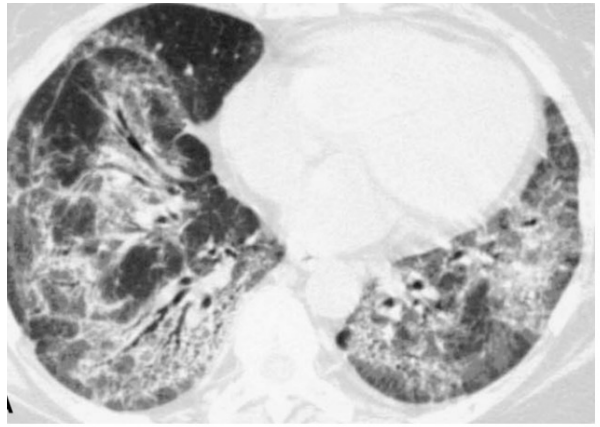
Constitutional symptoms
Proximal muscle weakness
Morning stiffness
Arthritis, arthralgias
Sicca symptoms
Dysphagia, GERD
Rashes
Raynaud’s

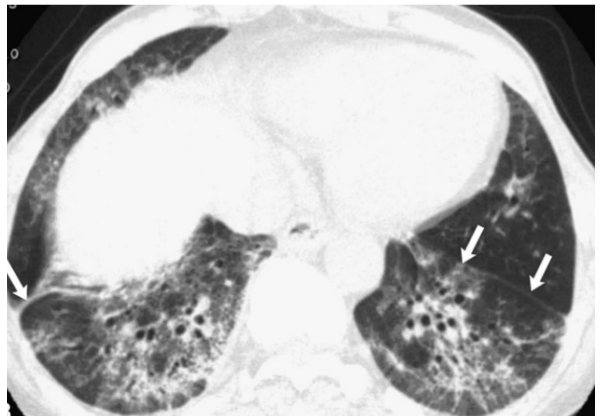
Physical Exam

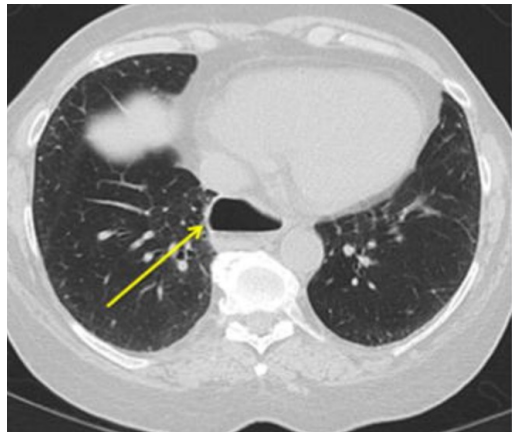
CT findings

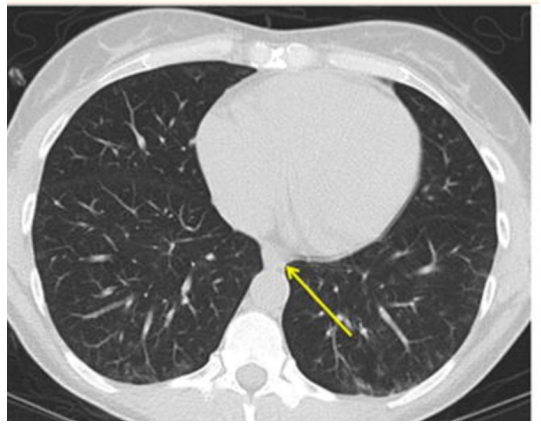
NSIP pattern





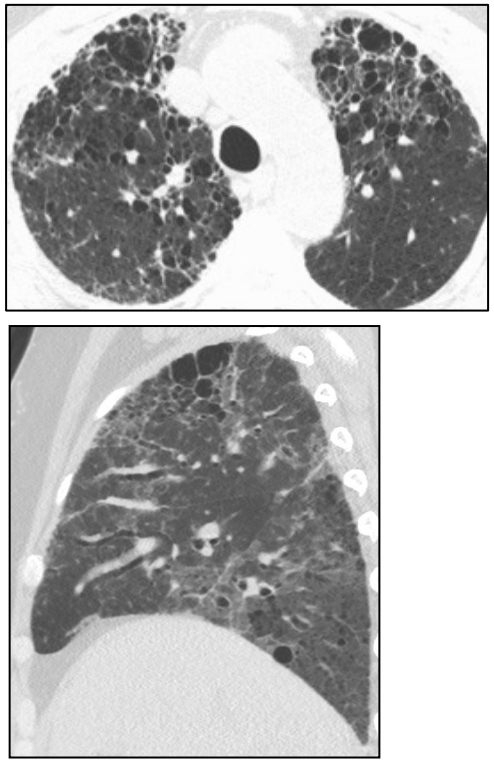
Esophageal dilation



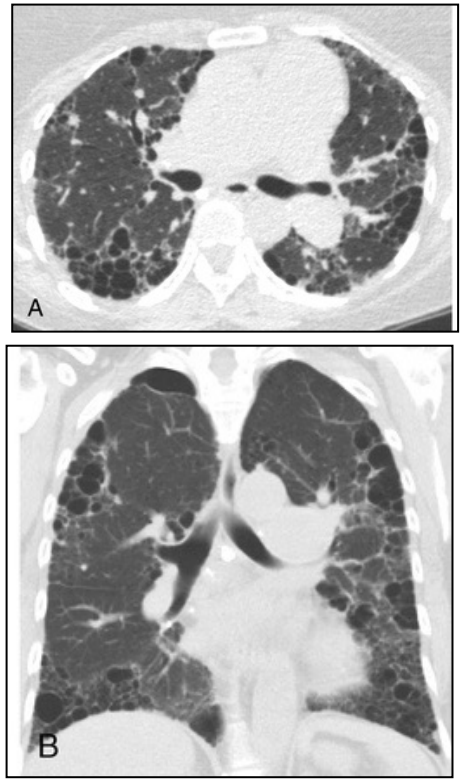


CT findings in CTD-UIP

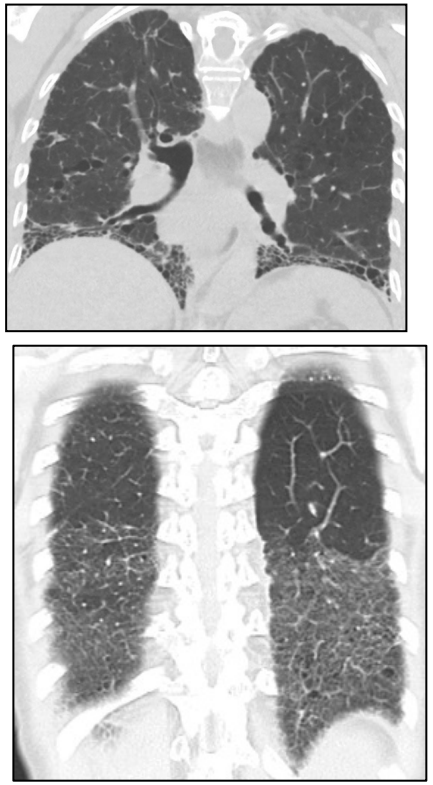
Anterior upper lobe



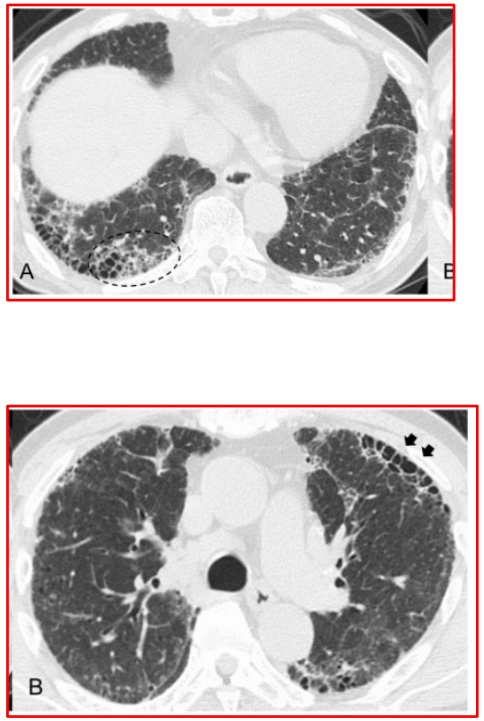
Exuberant honeycombing



Straight edge



Honeycombing in ANCA vasculitis



Chung et al. *American Journal of Roentgenology.* 2018
Chung et al J Comput Assist Tomogr 2021 Sep-Oct;45(5):776-781.

Yamakawa et al. BMC Pulm Med 2021 Nov 3;21(1):346.

Autoimmune Diseases associated with ILD

ANCA Associated Vasculitis (AAV-ILD)

CTD-ILD

- **Rheumatoid Arthritis (RA)**
- **Systemic sclerosis (SScl)**
- **Idiopathic Inflammatory Myopathies**
  - **Antisynthetase syndrome**
  - **Sjögren's, Mixed Connective Tissue Disease (MCTD), Systemic Lupus erythematosus**

Interstitial pneumonia with autoimmune features (IPAF)

ANCA-Associated Vasculitis

Microscopic polyangiitis (MPA) ILD in 45%
Granulomatosis with polyangiitis (GPA) ILD in 23%
Eosinophilic granulomatosis with polyangiitis (EGPA)
ANCA+ no systemic vasculitis

ILD: Mostly fibrotic, mostly UIP, can be OP, NSIP

Serologies: Antineutrophil cytoplasmic antibodies

Myeloperoxidase(MPO) Proteinase 3 (PR3)

Extrapulmonary: glomerulonephritis, nasal involvement

Other pulmonary pleurisy, nodules, alveolar hemorrhage

Kadura & Raghu Eur Respir Rev 2021 Nov 8;30(162; Yamakawa et al. J Clin Med. 2022 Jul; 11(13; BMC Pulm Med. 2021 Nov 3;21(1):346. Sebastiani Clin Exp Rheumatol. 2020 Mar-Apr;38 Suppl 124(2):221-231. Wallace & Stone Front Immunol 2019; Doliner et al Rheumatology 2022 Jun 14;

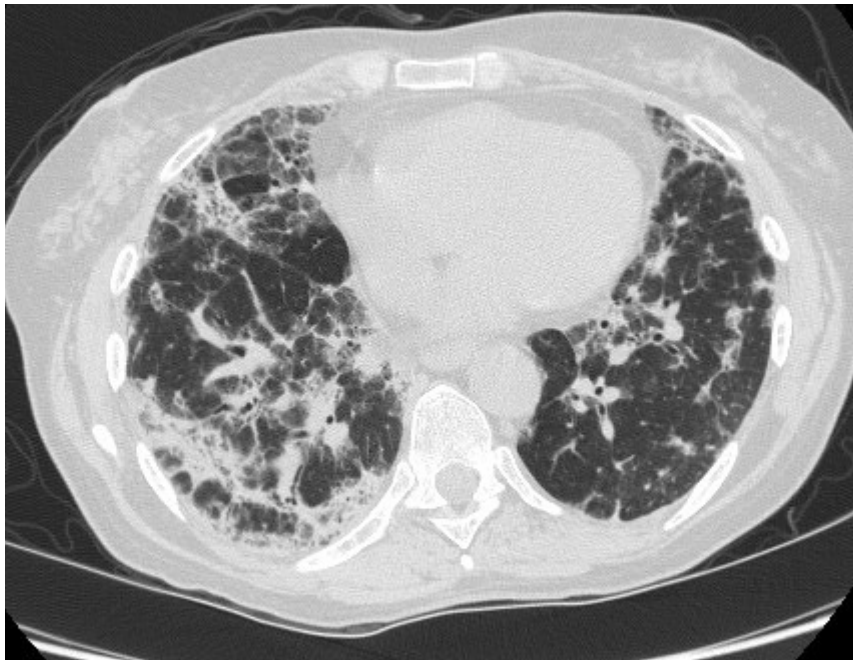
Rheumatoid Arthritis

ILD: Mostly UIP; NSIP, OP, bronchiolitis

Serologies: Rheumatoid factor, anti-CCP

Extrapulmonary: Joint deformity, nodules, morning stiffness

Other pulmonary bronchiectasis, bronchiolitis, nodules



Juge Eur Respir J 2021 Feb 11;57(2) Mathai and Danoff *BMJ* 2015, Mori et al. *Resp Med* 2012, Bongartz et al. *Arthritis & Rheumatism* 2010, Kouduri et al. *Rheum* 2010, Gochuico et al. *Arch Int Med 2008*,

Idiopathic Inflammatory Myopathies

Serologies: CK, aldolase

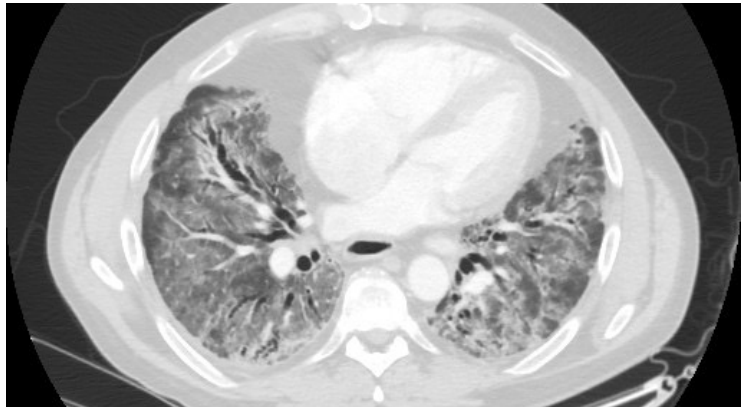
Myositis Specific/Associated Antibodies:

Mi-2, SRP, Ro-52/SSA, PM/Scl, Ku, **MDA-5**

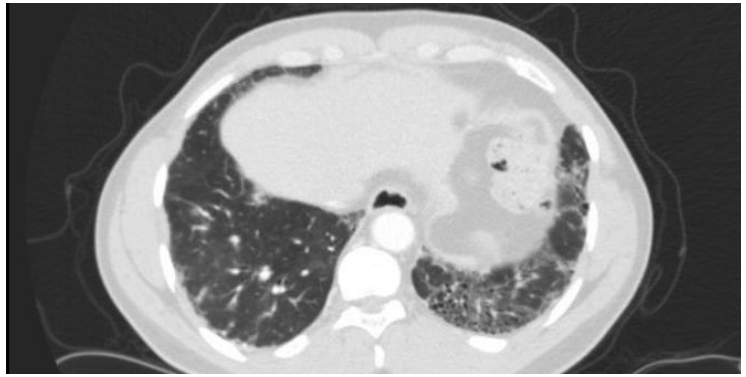
Extra pulmonary: Muscle weakness, Gottron's papules, heliotrope rash

Other pulmonary: acute pneumonitis/ARDS pneumomediastinum

Systemic symptoms may be subtle or delayed



51 year old + Ro/SSA



47 year old + MDA5

Hallowell &Paik Clin Exp Rheumatol 2022 Feb;40(2):373-383, Mehta et alBest Pract Res Clin Rheumatol. 2022 Jun;36(2); Long and Danoff Clin Chest Med. 2019 Sep;40(3):561-572.

Antisynthetase Syndrome

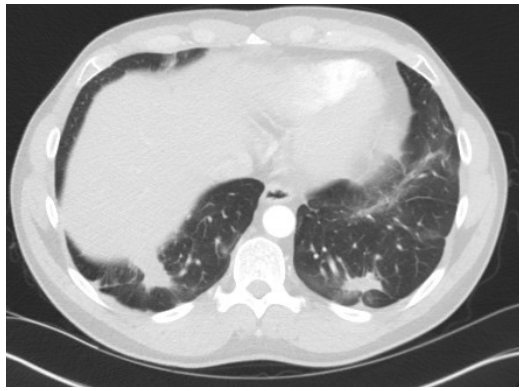
ILD: NSIP, UIP, OP

Serologies: Anti-aminoacyl-tRNA synthetase antibodies Anti-Jo-1, PL-7, PL-12, KS, OJ

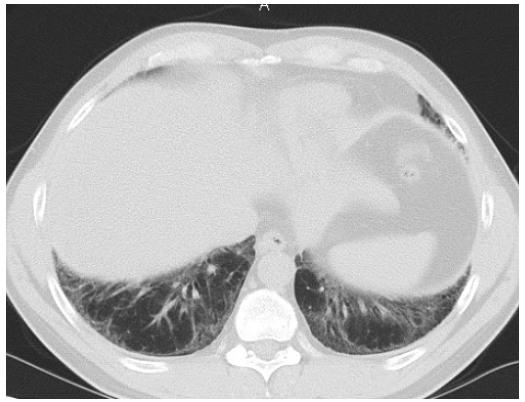
Extra pulmonary: Inflammatory myositis, GI involvement, polyarthritis, fevers, mechanic's hands

Other pulmonary: acute pneumonitis/ARDS

Clinical spectrum may vary by antibodies



41 year old + Jo-1

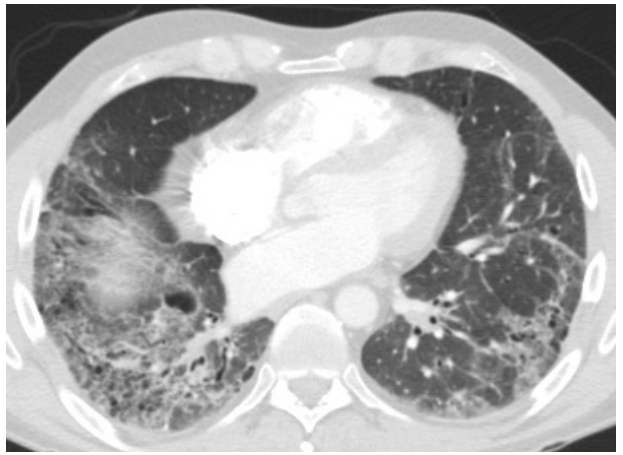


40 year old + PL-7

Hallowell &Paik Clin Exp Rheumatol 2022 Feb;40(2):373-383
Mehta et al Best Pract Res Clin Rheumatol 2022 Jun;36(2):101769

Systemic Sclerosis

ILD: NSIP, UIP



Serologies: ANA, centromere, anti-Scl-70, RNA polymerase III, anti-U2-RNP, PM-ScL, anti-Ku

Extra pulmonary: skin thickening
Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasias). ~4% lung disease is first symptom

Other pulmonary: Pulmonary hypertension

Walker et al Ann Rheum Dis 2007; **66**: 754–763
Cutolo Best Pract Res Clin Rheumatol 2013 Apr;27(2):237-48.

IPAF: Autoimmune-ish ILD

2 of 3 Clinical, Serologic, and Morphologic Domains and ILD

Clinical domain inflammatory arthritis, morning stiffness, digital ulcers, fissures, rash, swelling, telangiectasia

Serology: ANA >1:320, nucleolar or centromere pattern, RF >= 2x, CCP, dsDNA, Sm, SSA/Ro; SSB/La, RNP, ScL-70, PM-Scl, antisynthetase, MDA5

Morphology:

Radiology or Pathology : NSIP, OP, NSIP/OP, LIP
UIP pattern compatible, does not count towards diagnosis
Pathology: lymphoid aggregates, lymphoplasmacytic infiltrates
Multicompartment: airway disease, vasculopathy, pleural or pericardial effusions or thickening

Graney and Fischer *Ann Am Thorac Soc.* 2019 Adegunsoye et al. *AM J Path* 2017, Fisher et al. *Eur Respir J*. 2015

Anti-inflammatory treatment

Steroids: Most common first agent especially for RA, myositis

Typically start at 0.5-1 mg/kg. Pulse 1 gram if severe

Mycophenolate mofetil (MMF): steroid sparing, slower onset

Scleroderma Lung Study II. MMF up to 1.5 bid x 2 yr vs.cyclophosphamide x 1 yr
Similar efficacy (2% increase FVC)

Typically start at 500 mg bid, increase to 1500 mg bid max

Rituximab: 1 gram day 1 and day 14

IVIG: Recommended for refractory myositis; used for acute cases; 2 gram/4-5 days

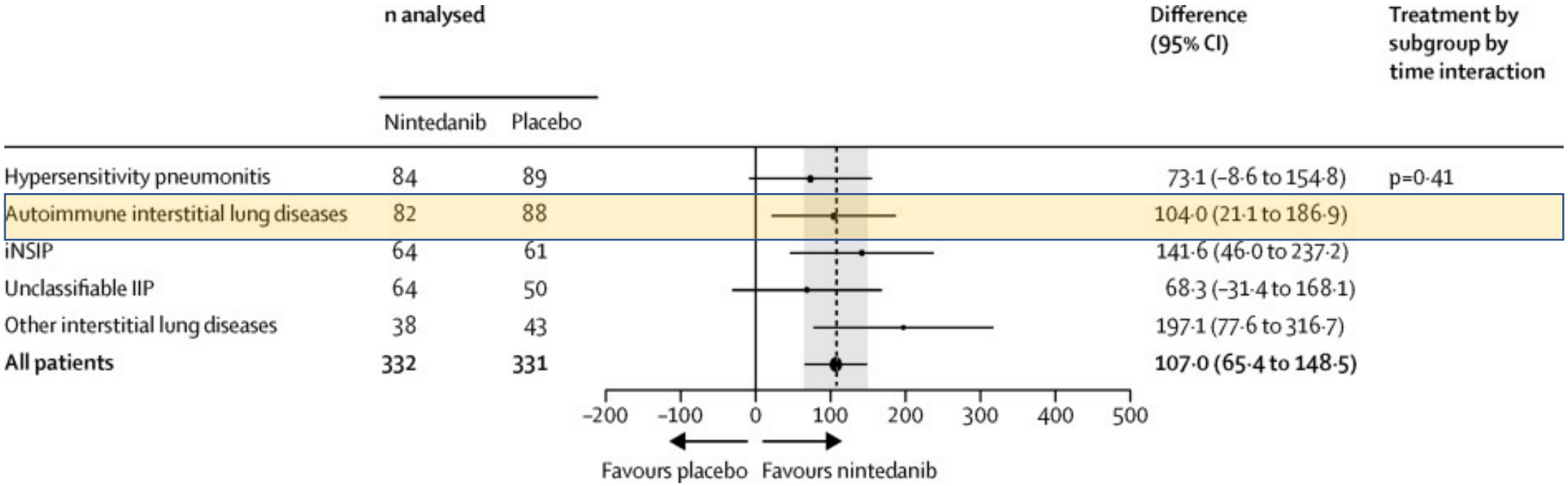
Tacrolimus: goal level 5-8 ng/mL

Hallowell &Paik Clin Exp Rheumatol 2022 Feb;40(2):373-383, Fischer et al Arthritis Rheumatol. 2019 Feb;71(2):182-195.Wilfoong Ther Adv Musculoskelet Dis. 2021

Anti-fibrotic treatment: Nintedanib

SENSCIS trial: Nintedanib for systemic sclerosis

INBUILD trial 2019: Nintedanib for all progressive fibrotic ILD



Distler et al N Engl J Med 2019 Jun 27;380(26):2518-2528.Wells et al. Lancet Respir Med 2020 May;8(5):453-460. Wilfoong Ther Adv Musculoskelet Dis. 2021; Allanore Ann Rheum Dis 2022 Aug 16

Anti-fibrotic treatments: Pirfenidone

LOTUSS – suggested tolerability in SSc

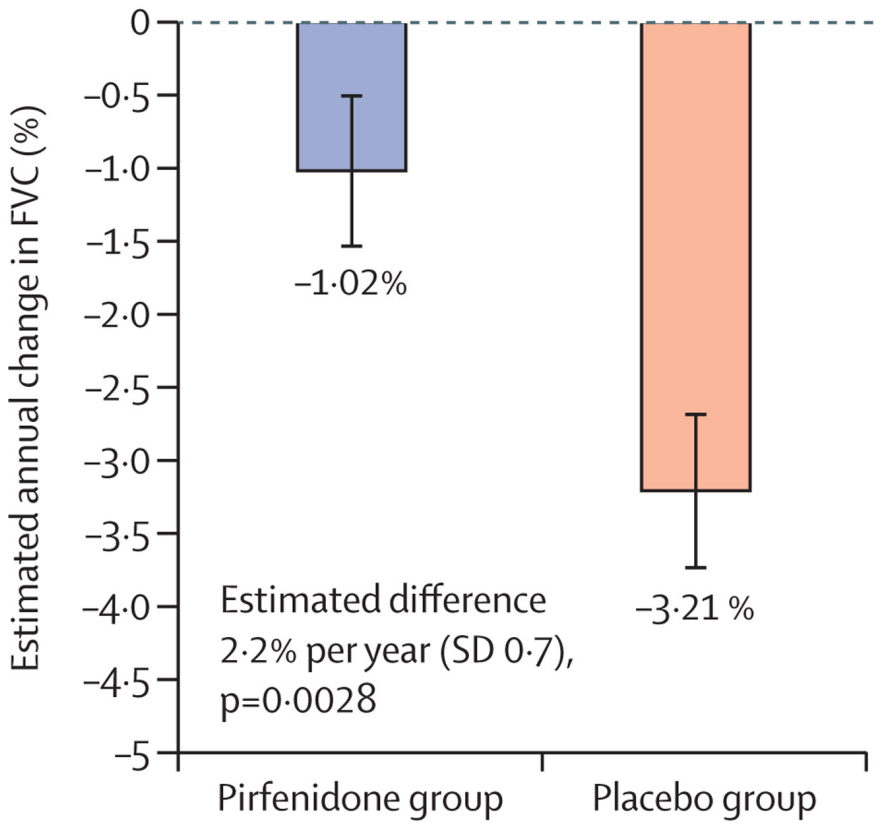
SLS III – pirfenidone and MMF *ongoing*

<u>TRAIL trial in RA-ILD</u>

Stopped early- slow recruitment

Primary outcome - % patient with 10% decline or death – no difference

Secondary – statistically significant difference in decline



Lung Transplant in CTD

ISHLT Consensus 2021

Similar outcomes to IPF

No higher risk of chronic rejection/CLAD

Specific guidance for evaluation

Concomitant renal failure, cardiomyopathy

Profound esophageal issue and unable to be NPO

Atlantoaxial instability

Refractory arthropathy

Severe muscle weakness

Thank you

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