ILD Collaborative

Project ECHO

Myositis-associated ILD: update on treatment approaches and challenges

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Disclosures

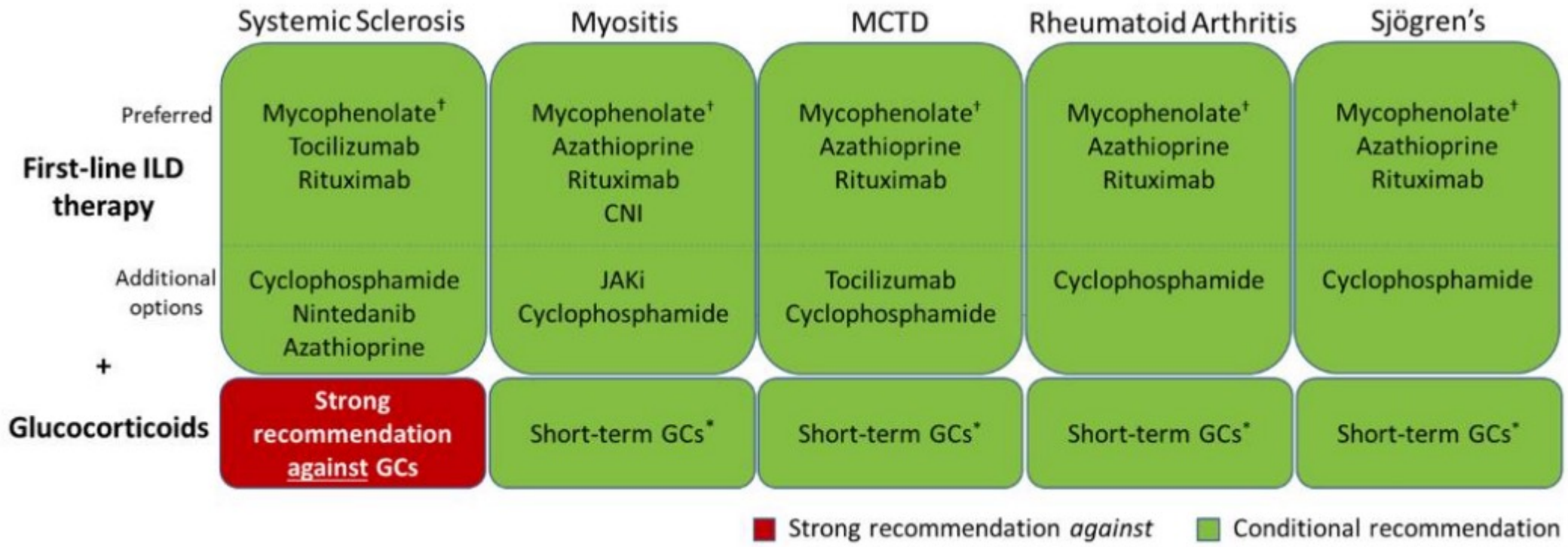
- Speaking and consulting fees from Boehringer Ingelheim, Genentech, Vicore
- Research trials with Boehringer, Genentech, Galapagos, Hoffmann-La Roche, Nitto Denko
- Authorship fees from UpToDate, Dynamed

ILD is common in patients with myositis

- Reported prevalence in DM/PM is 20% -78%
- Reported prevalence with anti-synthetase antibodies is 71-100%
- **ILD precedes the diagnosis of myositis in 13% to 37.5% of patients**

Marie et al. Arthritis Rheum 2011;63:3439-47.
Chen et al. Clin Rheumatol 2009;28:639-46
Yu et al. Clin Rheumatol 2011;30:1595-601
Hamaguchi et al. PLoS ONE 2013;8(4):e60442

2023 American College of Rheumatology (ACR) Guideline for the Treatment of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Disease (SARD)



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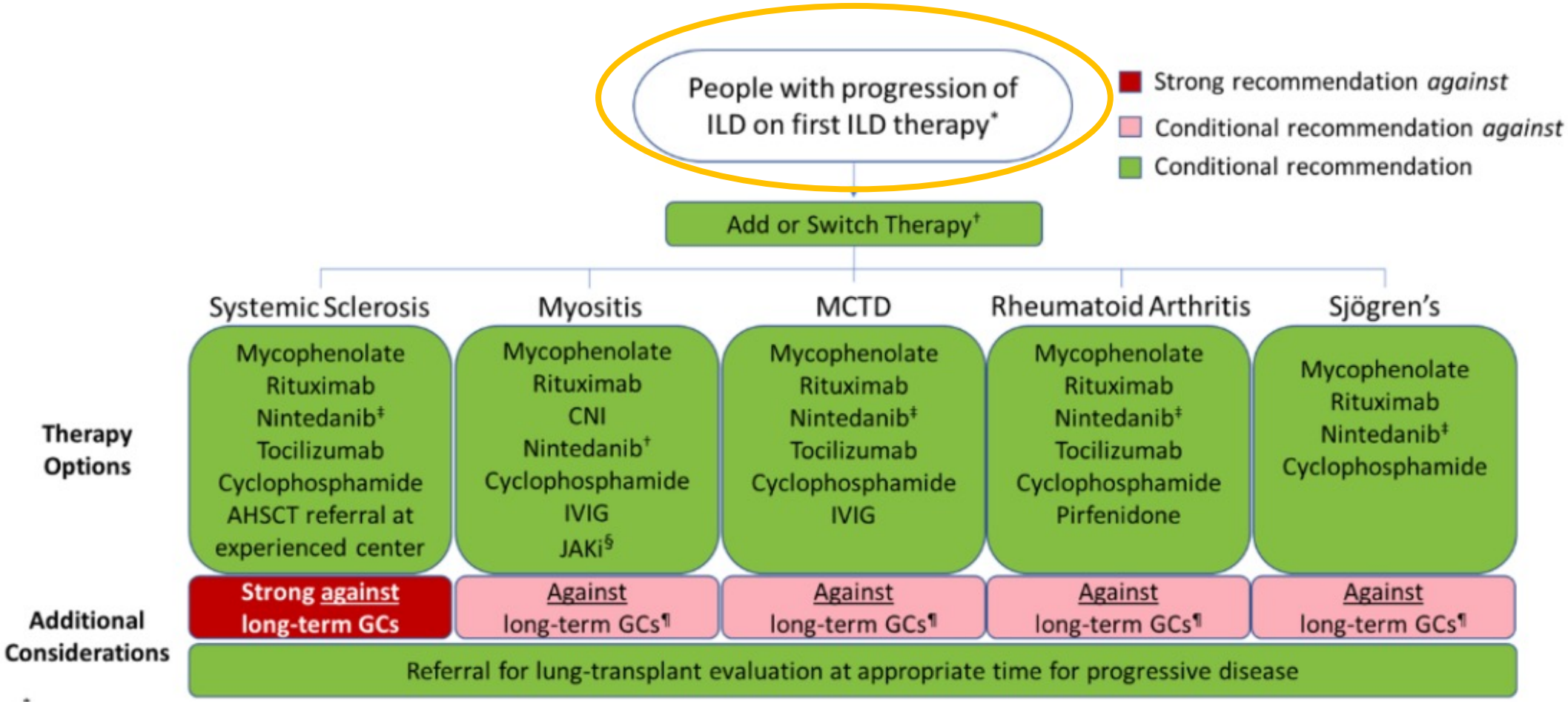
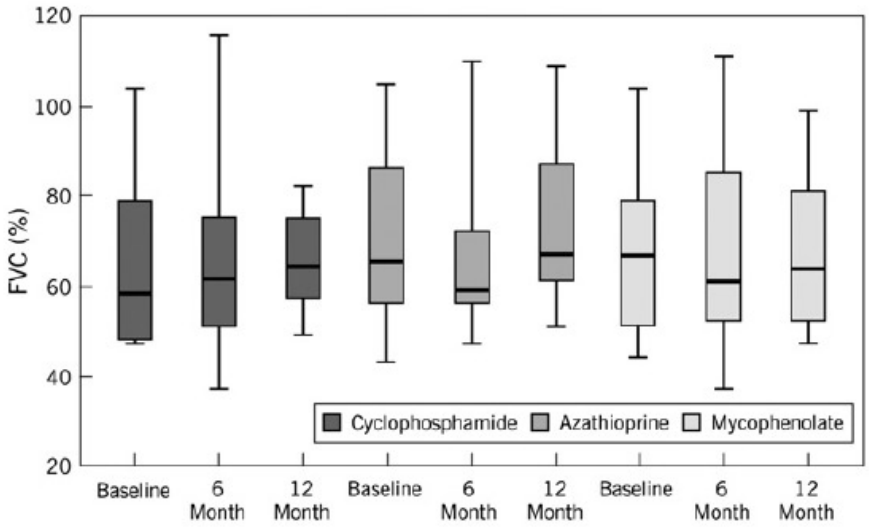


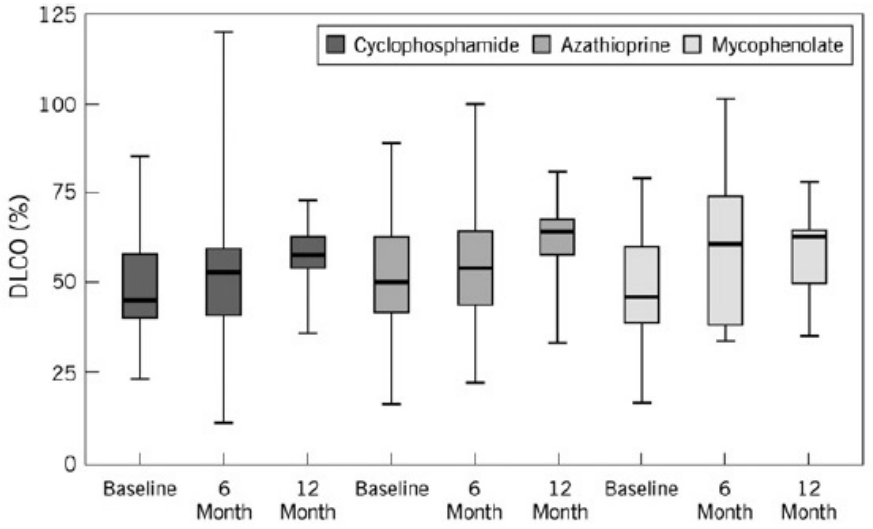
Myositis-ILD can be stabilized by a variety of agents

46 patients with PM/DM-ILD (50% had Jo-1)

- Cyclophosphamide 24
- Azathioprine 13
- Mycophenolate 9



FVC increased by 5%

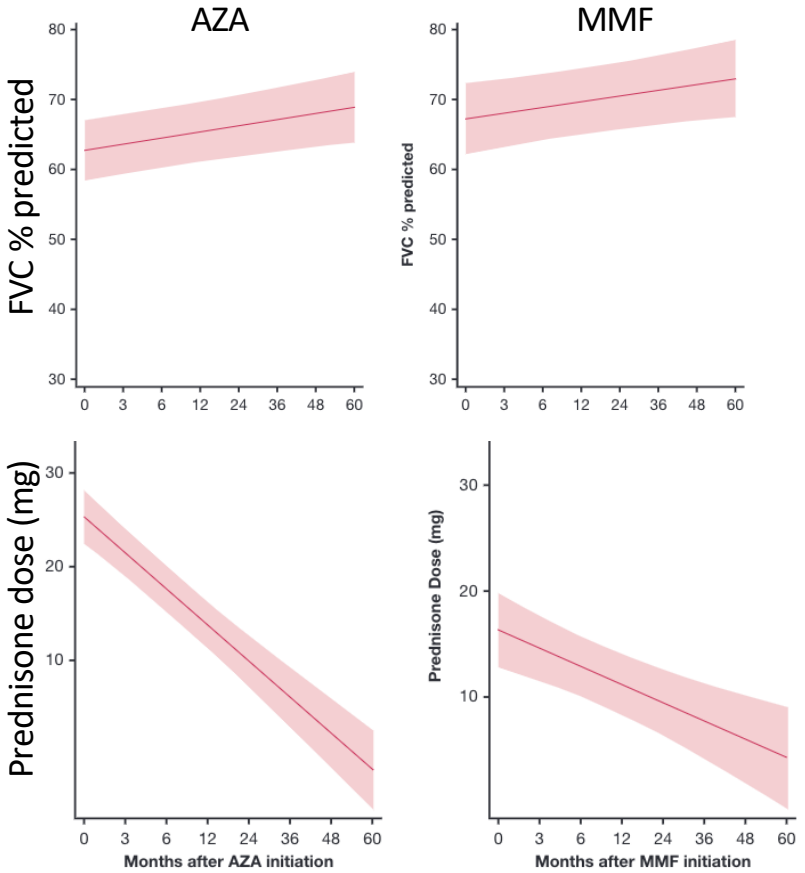


DLCO increased by 2.9%

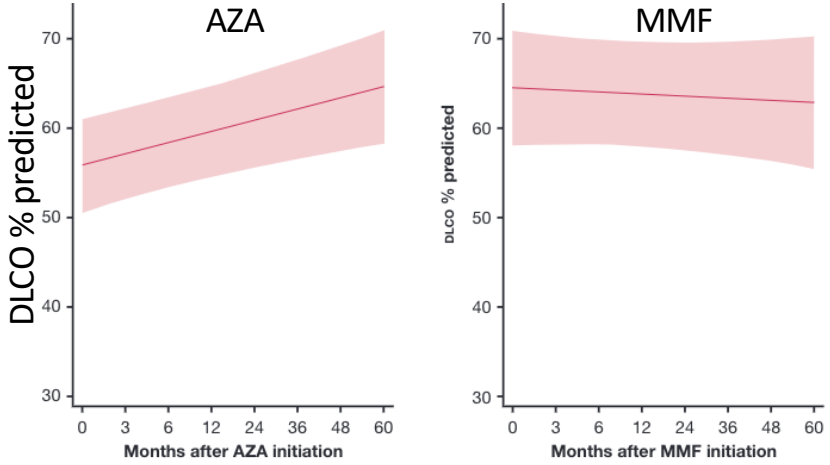
Ave prednisone dose: 40 mg/d pre-treatment; 10-16 mg/d at 6 months; 7.5 mg/d at 12 months

Mira-Avendano et al. *Respiratory Medicine* (2013) 107, 890e896

Azathioprine vs Mycophenolate in myositis-ILD



Retrospective study
66 received AZA
44 received MMF



Ave prednisone dose at initiation: 28 (AZA) vs 18 (MMF)
AZA group had more adverse events: LFTs, cytopenias, GI symptoms (33% vs 13%)

Huapaya et al. *CHEST* 2019; 156(5):896-906

Tacrolimus for refractory myositis-ILD

54 patients with myositis-ILD received prednisone plus AZA, MTX, or MMF
~ 50% had an anti-synthetase Ab

Response to conventional Tx (57%)
PM-ILD 67%
DM-ILD 35% *p = 0.013*

23 patients (43%) failed to respond to conventional therapy
⟶ Received add-on therapy with either CYC (5) or tacrolimus (18)

Response to tacrolimus
ILD improved in 94%

Decrease in prednisone
At 3-6 months 65%
At 12 months 81%

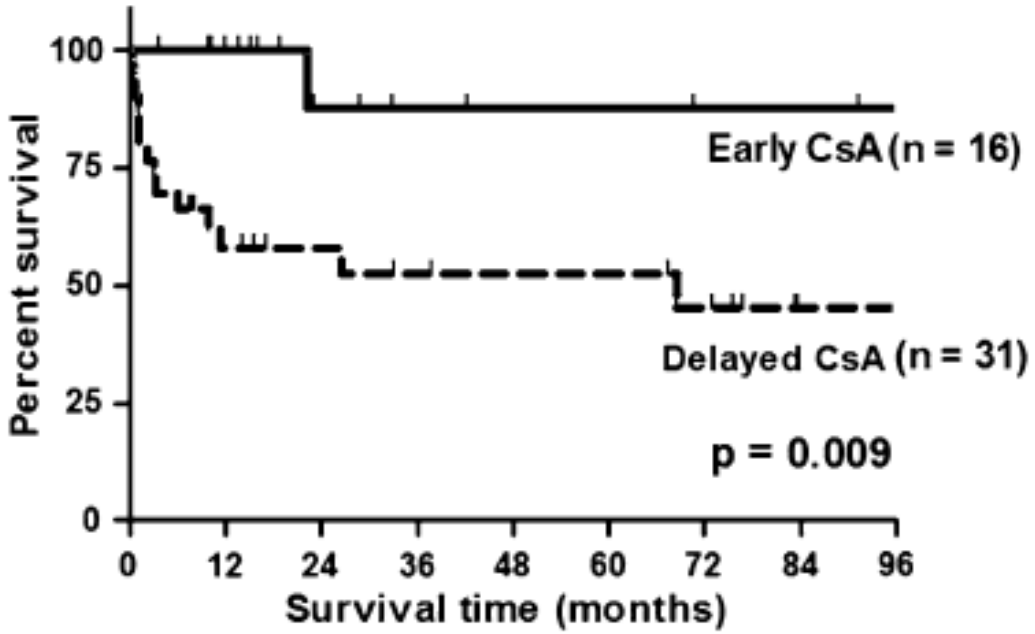
Timing of calcineurin inhibitors may matter for myositis-ILD

47 DM-ILD patients who ultimately received CsA (all received steroids)

Early Tx = within two weeks

Delayed Tx = Ave 5.3 mo after ILD dx

- Often received other steroid-sparing agents first

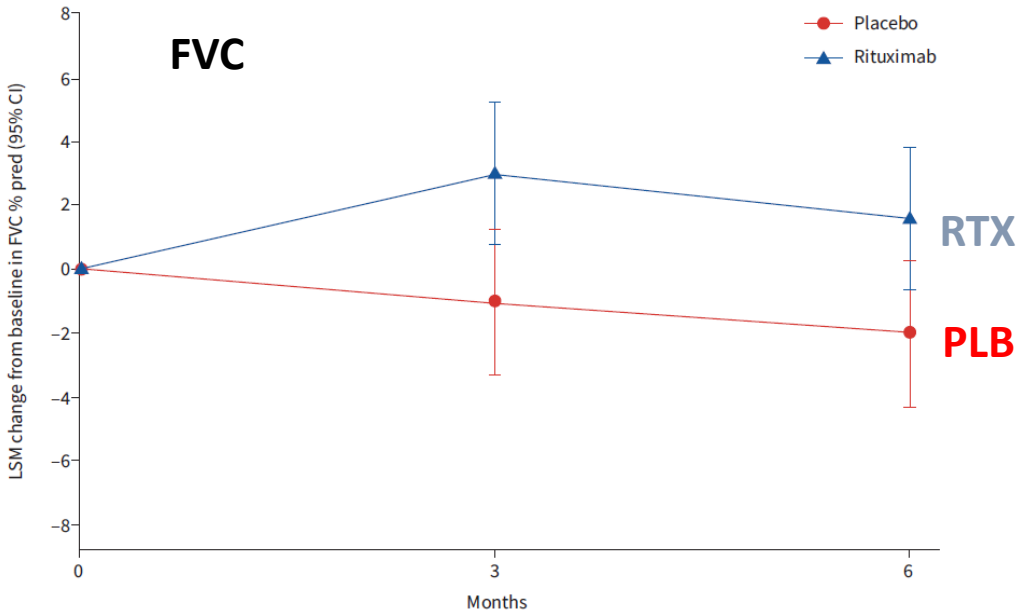


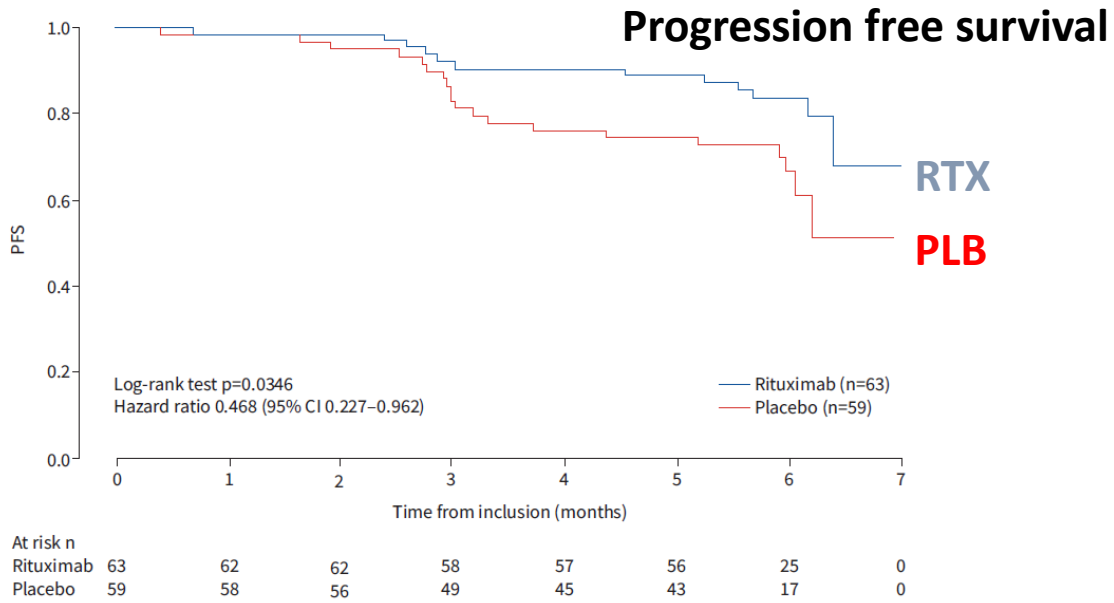
*Rate of CADM higher in early group
62.5% vs 29% *(p = 0.34)*

Go et al. *Rheumatol Int* (2016) 36:125–131

Rituximab and mycophenolate mofetil combination in patients with interstitial lung disease (EVER-ILD): a double-blind, randomised, placebo-controlled trial

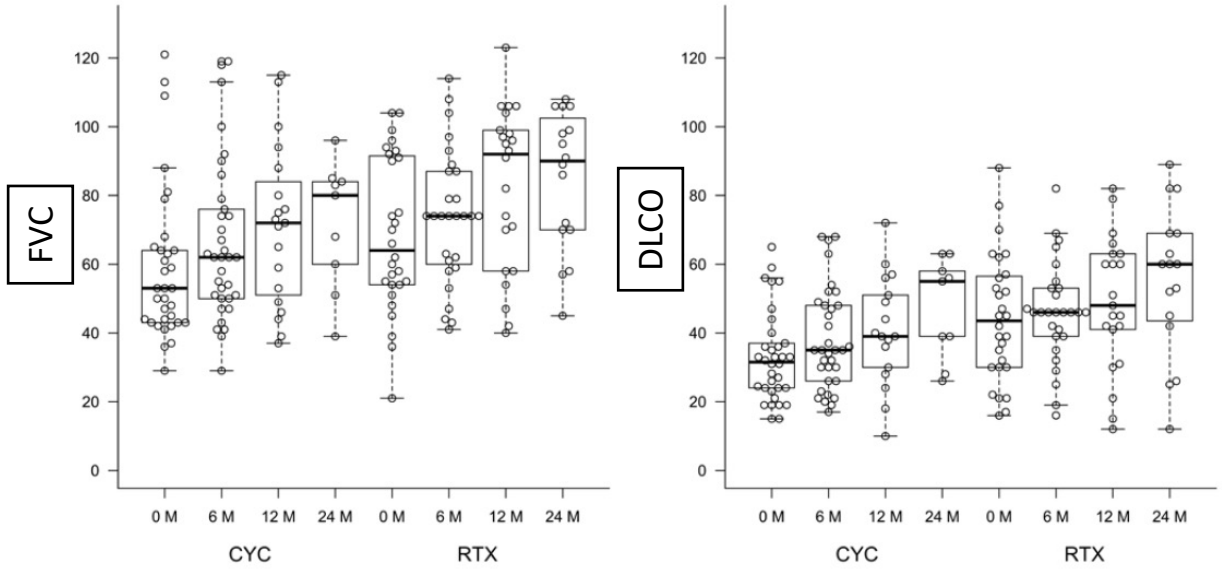
- All had an NSIP pattern of disease (CTD, IPAF, or idiopathic)
- MMF 2g daily + Rituximab/Placebo for 6 months
- 63 received RTX; 59 received placebo



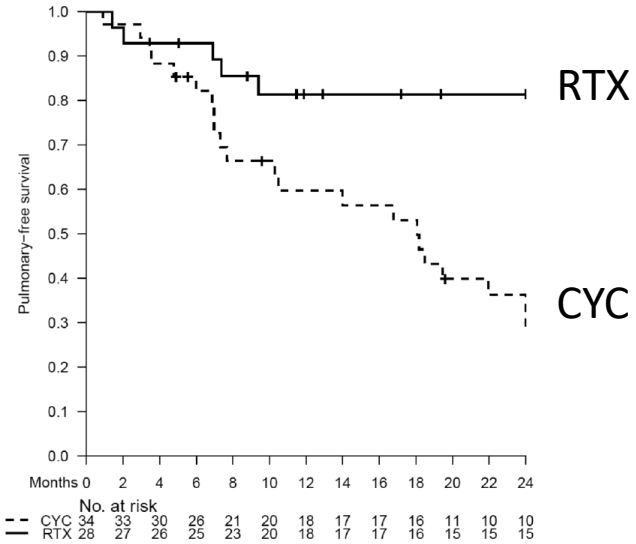


RTX vs CYC for antisynthetase associated-ILD

CYC 34 patients (88% received subsequent steroid-sparing agents)
RTX 28 patients (54% received subsequent steroid-sparing agents)



Pulmonary-free survival



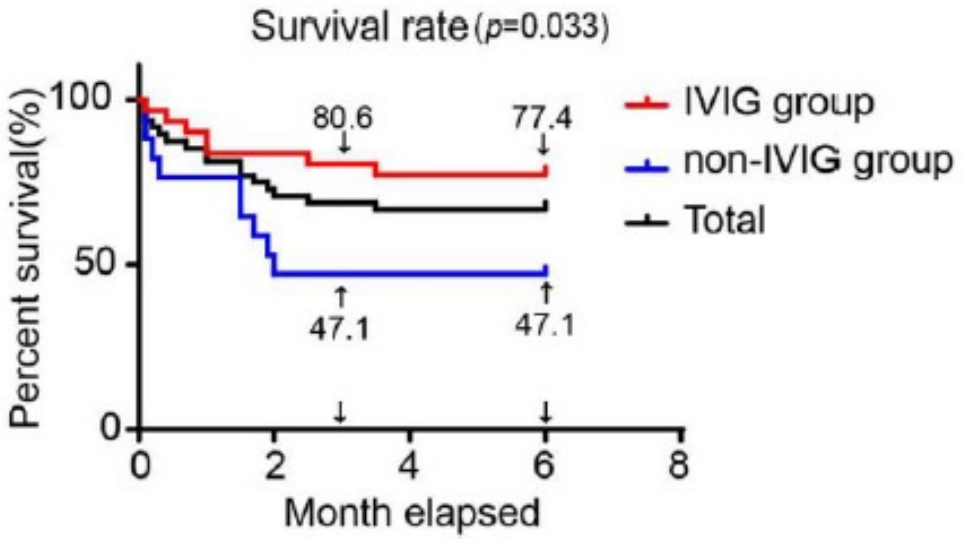
*CYC has statistically significant lower FVC and DLCO at baseline

IVIg for treating myositis-ILD

Retrospective review of patients with MDA5+ RP-ILD

17 patients received standard therapy (CYC, CNI, RTX, Tofac)

31 patients received IVIG + standard therapy



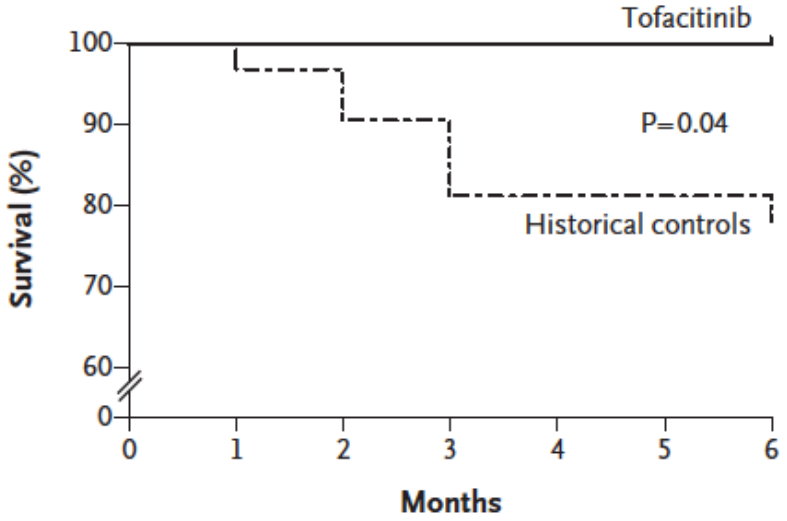
Remission rate at 3 months:

IVIG 71%

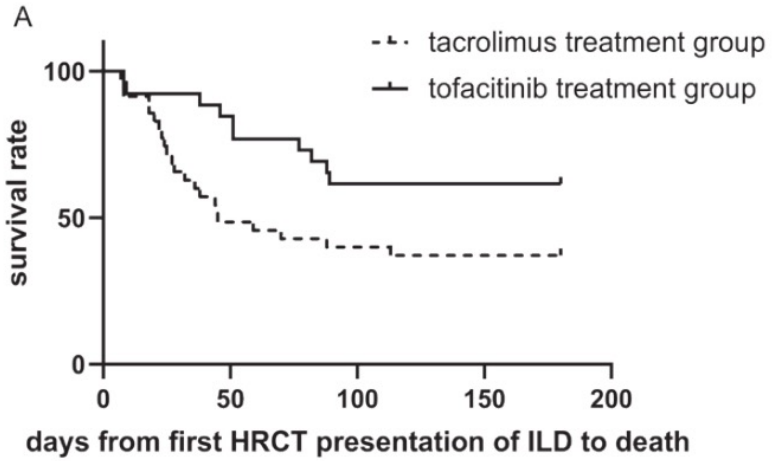
Standard therapy 41.2% p = 0.044

Tofacitinib for MDA5-ILD

18 pts received Tofacitinib vs 32 historical controls
-- ILD for less than 3 months
-- Well matched for disease severity



26 patients received TOF; 35 received TAC
--Groups were relatively well matched
--More Ro52 in TOF group
--More high-titer MDA-5 in TAC group



Mortality rates TOF vs TAC groups
6-month (38.5% vs 62.9%; *P* = 0.03)
1-year (44.0% vs 65.7%; *P* = 0.03)

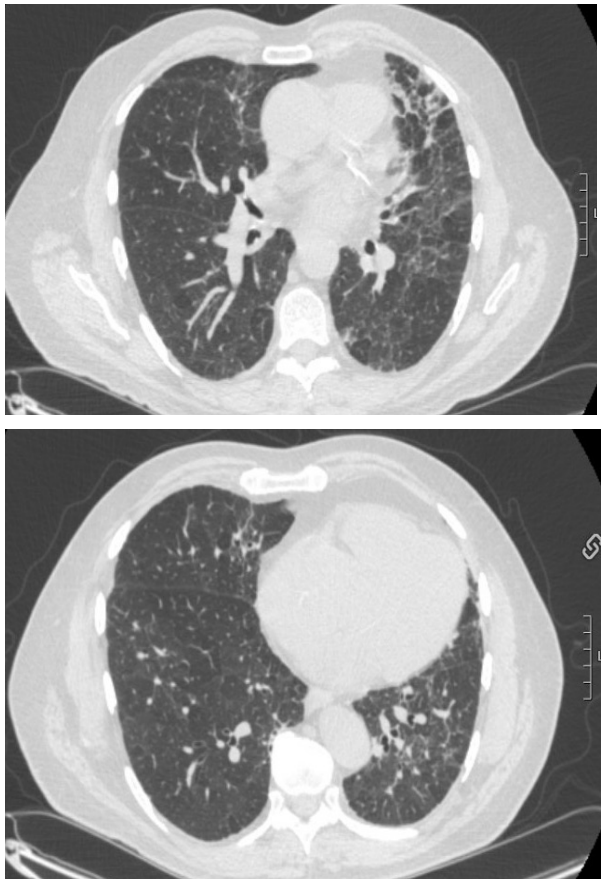
Chen et al. *NEJM* 2019; 381:3

Fan et al. *Journal of Rheumatology* 2022;49:1356–64

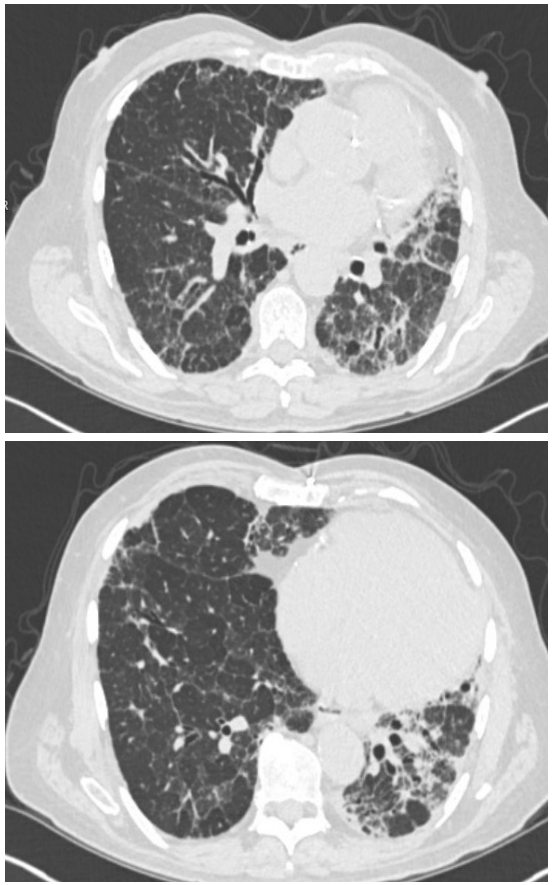
Myositis patients can develop a progressive fibrotic phenotype

62 M with anti-Jo-1 associated DM on low-dose prednisone and MMF

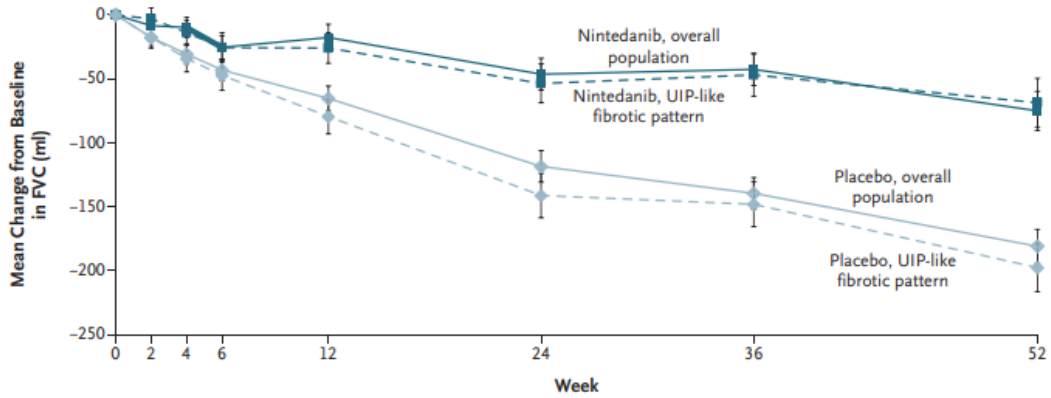
2019



2021



INBUILD — Nintedanib is effective for patients with PF-ILD (non-IPF)

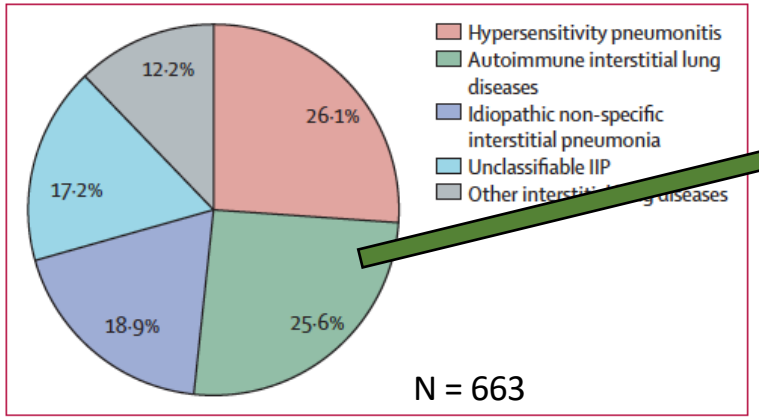


No. of Patients								
Overall population								
Nintedanib	332	326	320	322	314	298	285	265
Placebo	331	325	326	325	320	311	296	274
Patients with UIP-like fibrotic pattern								
Nintedanib	206	203	200	199	193	180	171	160
Placebo	206	202	202	201	197	190	176	162

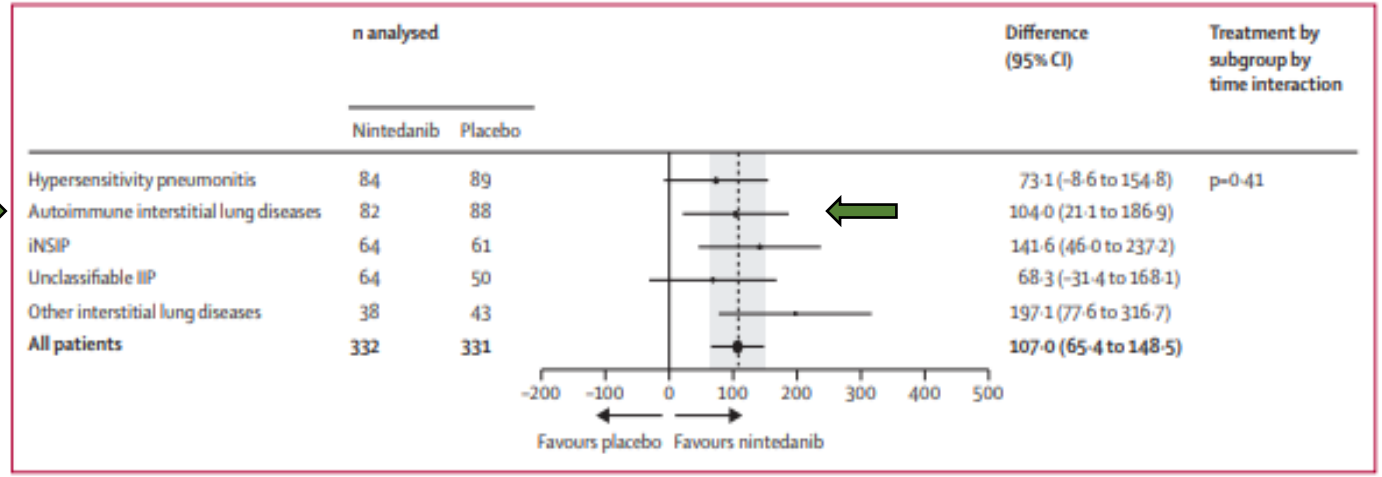
Table 2. Efficacy End Points.*

End Point	Nintedanib (N=332)	Placebo (N=331)	Difference (95% CI)
Primary end point			
Rate of decline in the FVC at 52 wk — ml/yr†			
Overall population	−80.8±15.1	−187.8±14.8	107.0 (65.4 to 148.5)‡
Patients with a UIP-like fibrotic pattern	−82.9±20.8	−211.1±20.5	128.2 (70.8 to 185.6)‡
Patients with other fibrotic patterns	−79.0±21.6	−154.2±21.2	75.3 (15.5 to 135.0)§

The INBUILD trial included RA but not myositis patients



Subgroup analysis of 25.6% (170) autoimmune patients:
--13.4% of patients had RA-ILD
--3.4% had other autoimmune ILD (myositis not specified)
--Difference in FVC decline vs placebo 104 mL/year



Wells et al. *Lancet Respir* Med 2020

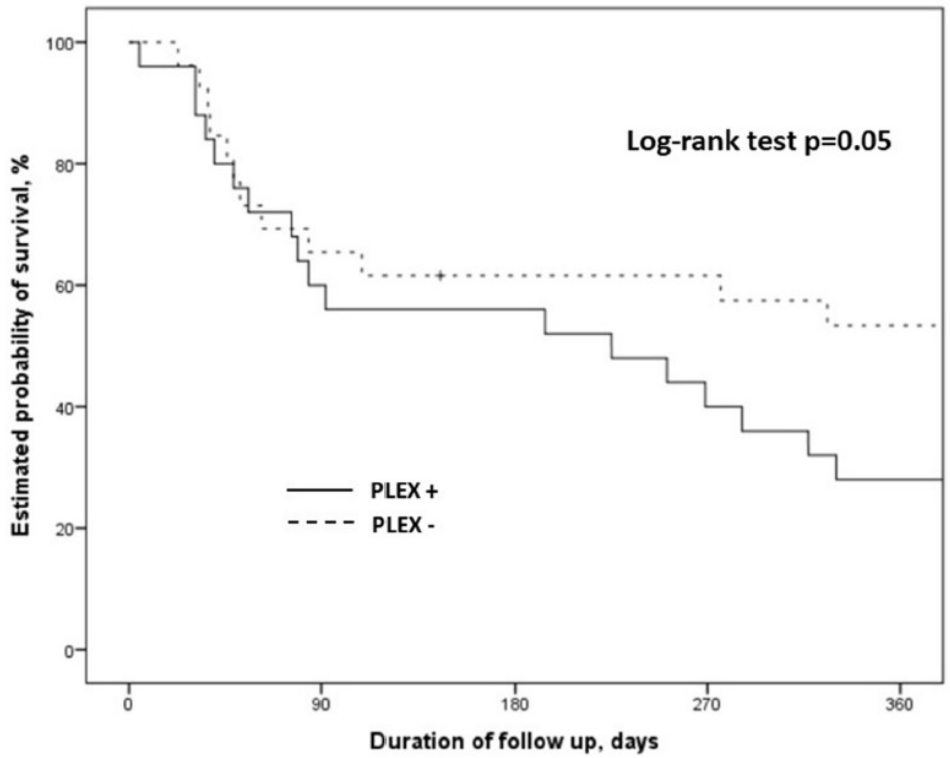
Plasma Exchange for RP-ILD

- 51 patients with anti-MDA5 RP-ILD
- 25 (49%) PLEX; 26 (51%) only immunosuppression
- PLEX patients were sicker
  (ventilator rate 76% vs 50%, p = 0.05)

One-year survival:

PLEX 20%

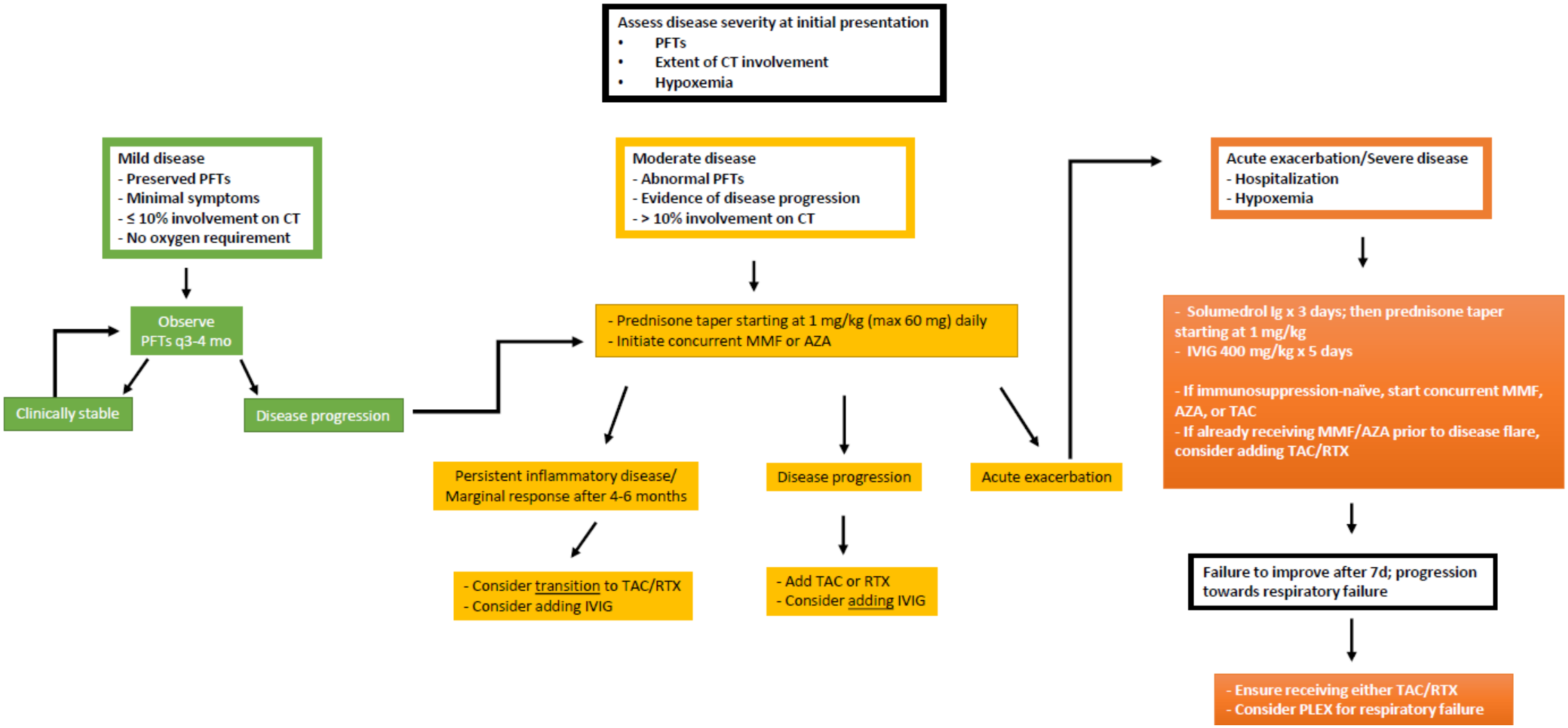
Immunosuppression only 54%



	Day	0	90	180	270	360
Patients at risk, n	PLEX+	25	15	14	10	7
	PLEX-	26	17	15	15	13

Fig. 2. Kaplan-Meier Curves for the One-Year Transplant-Free Survival According to the use of Plasma Exchange.

Treatment algorithm



RW Hallowell and SK Danoff. *Chest* 2023 Jun;163(6):1476-1491.

Summary

- Standard therapy for the treatment of myositis-ILD involves the use of steroid-sparing agents
- There is no strong data to suggest that one agent is superior to another!
- Although antifibrotics are routinely used in patients with a progressively fibrotic component, this practice is not based on strong clinical data
- Clinical trials are needed to guide our understanding of how best to care for this complex patient population