

# **Myositis-associated ILD: update on treatment approaches and challenges**

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# Disclosures

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- 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

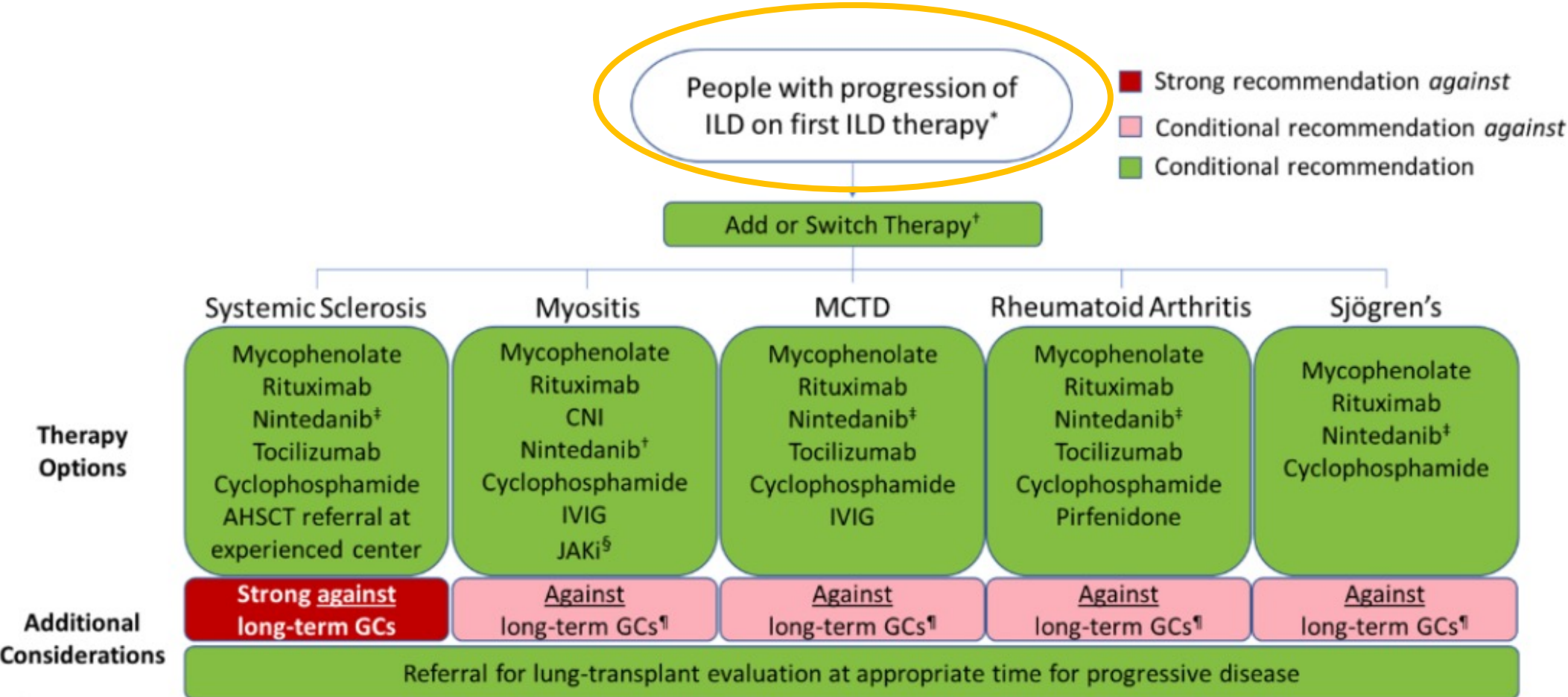
- Reported prevalence in DM/PM is 20% -78%
- Reported prevalence with anti-synthetase antibodies is 71-100%
- **ILD precedes the diagnosis of myositis in 13% to 37.5% of patients**

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

	Systemic Sclerosis	Myositis	MCTD	Rheumatoid Arthritis	Sjögren's
<b>Preferred First-line ILD therapy</b>	Mycophenolate <sup>†</sup> Tocilizumab Rituximab	Mycophenolate <sup>†</sup> Azathioprine Rituximab CNI	Mycophenolate <sup>†</sup> Azathioprine Rituximab	Mycophenolate <sup>†</sup> Azathioprine Rituximab	Mycophenolate <sup>†</sup> Azathioprine Rituximab
<b>Additional options</b>	Cyclophosphamide Nintedanib Azathioprine	JAKi Cyclophosphamide	Tocilizumab Cyclophosphamide	Cyclophosphamide	Cyclophosphamide
<b>+ Glucocorticoids</b>	<b>Strong recommendation against GCs</b>	Short-term GCs*	Short-term GCs*	Short-term GCs*	Short-term GCs*

■ Strong recommendation *against*     ■ Conditional recommendation

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



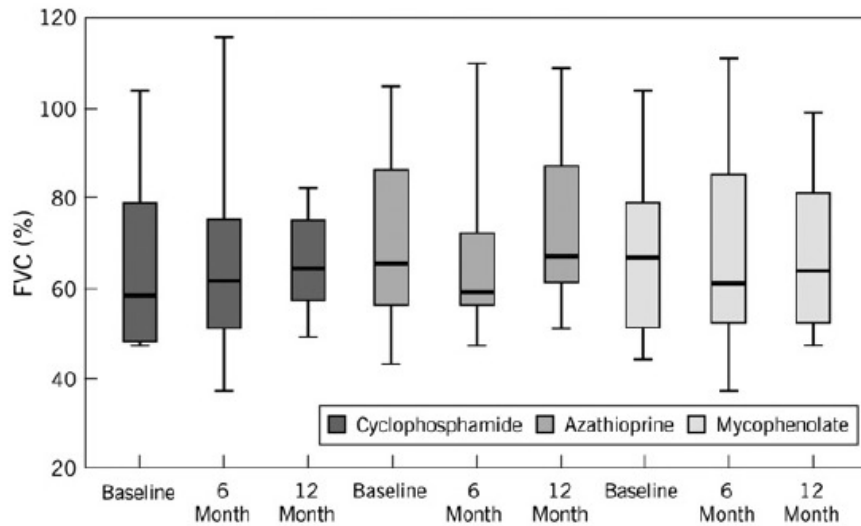
# Myositis-ILD can be stabilized by a variety of agents

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

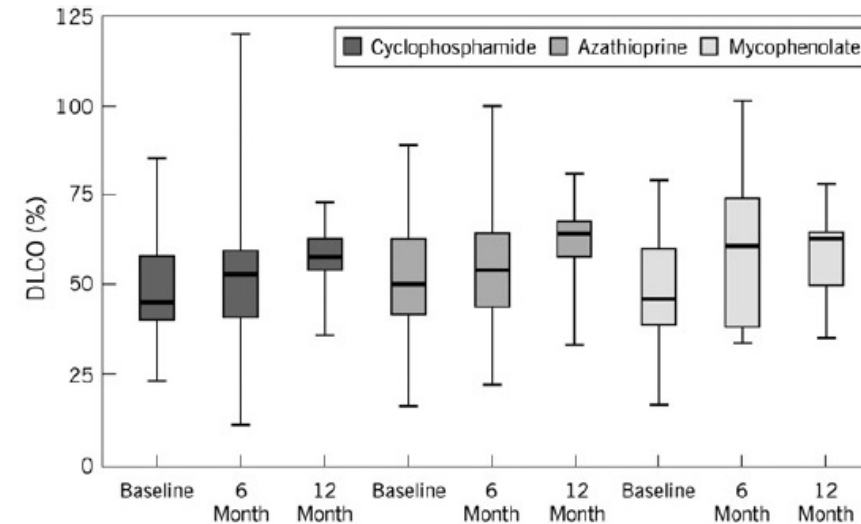
Cyclophosphamide 24

Azathioprine 13

Mycophenolate 9



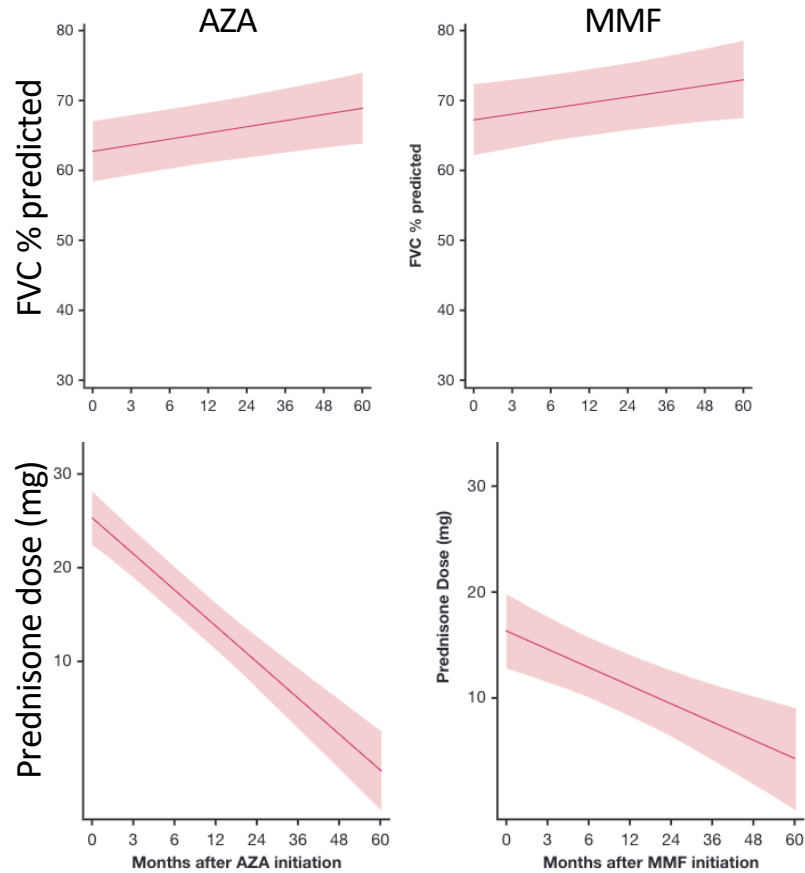
FVC increased by 5%



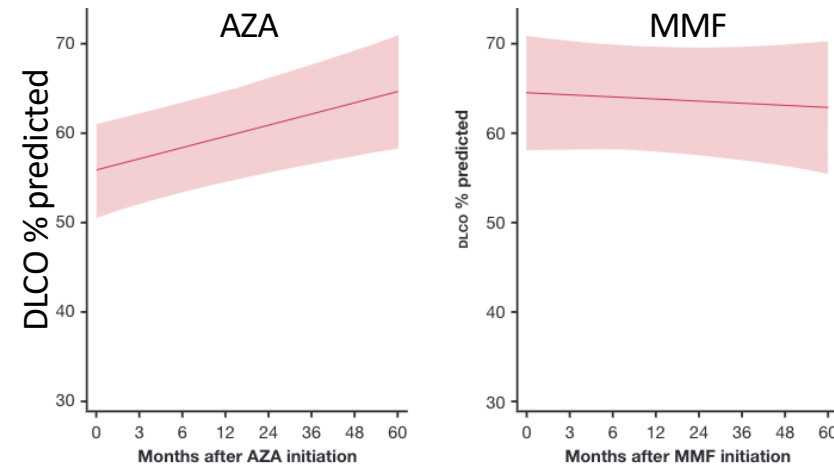
DLCO increased by 2.9%

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

# 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%)

# 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%



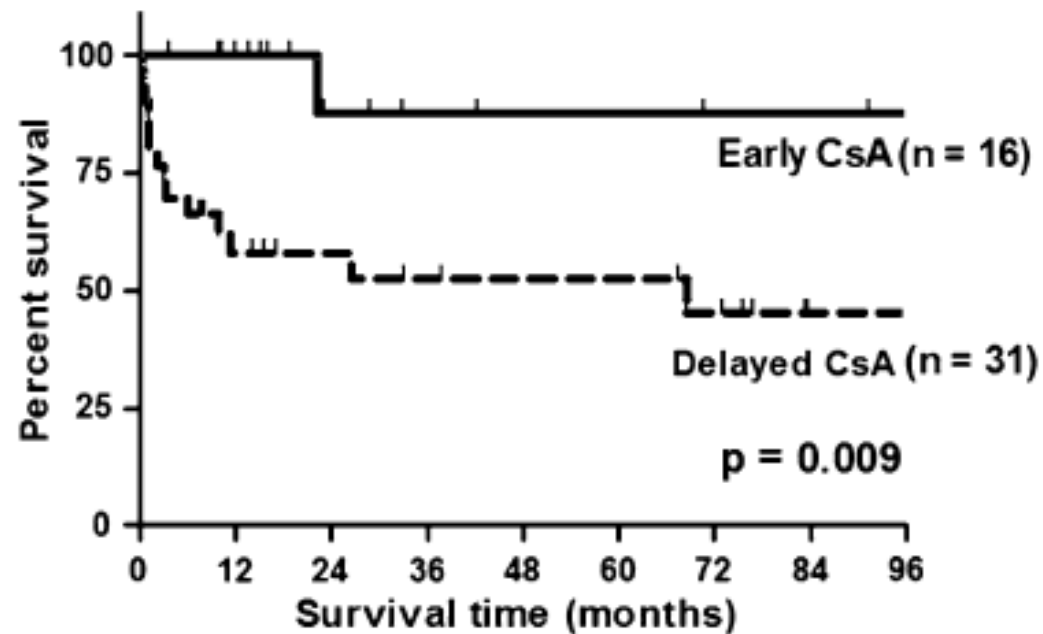
# Timing of calcineurin inhibitors may matter for myositis-ILD

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

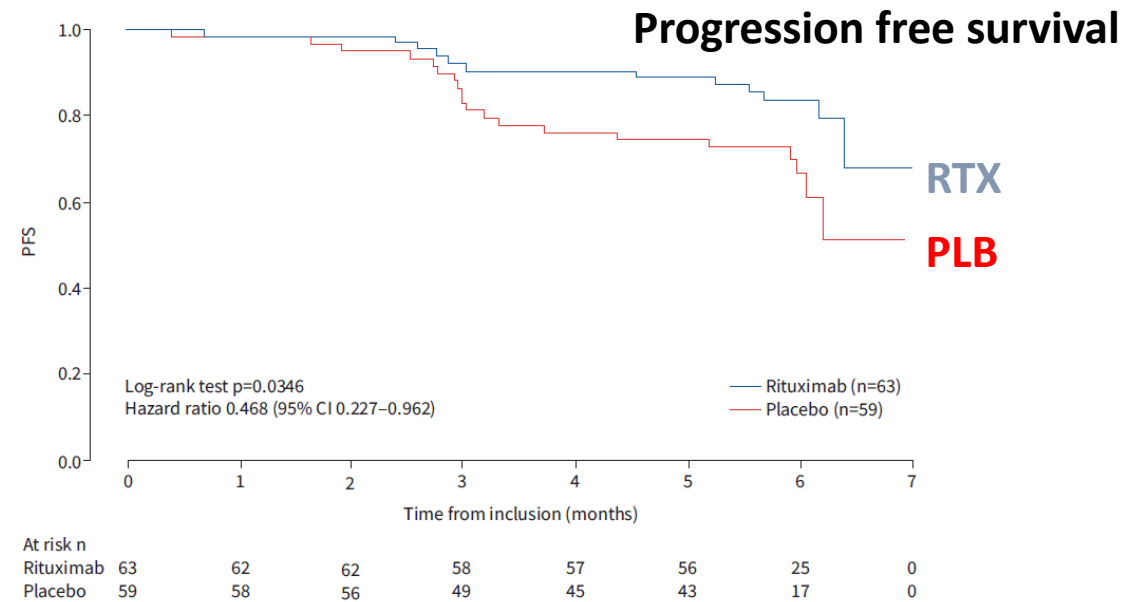
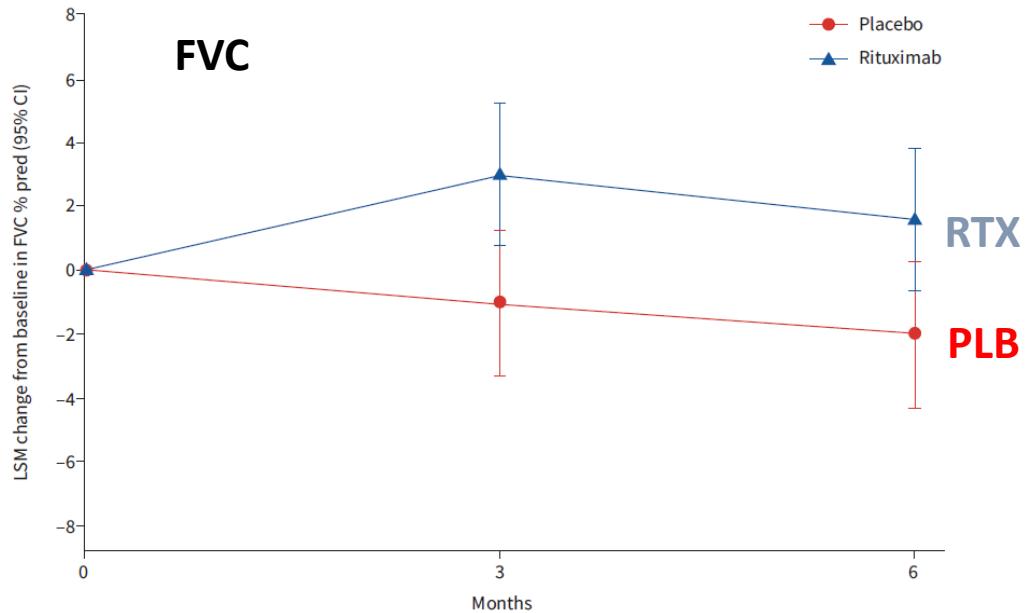
- Often received other steroid-sparing agents first



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

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

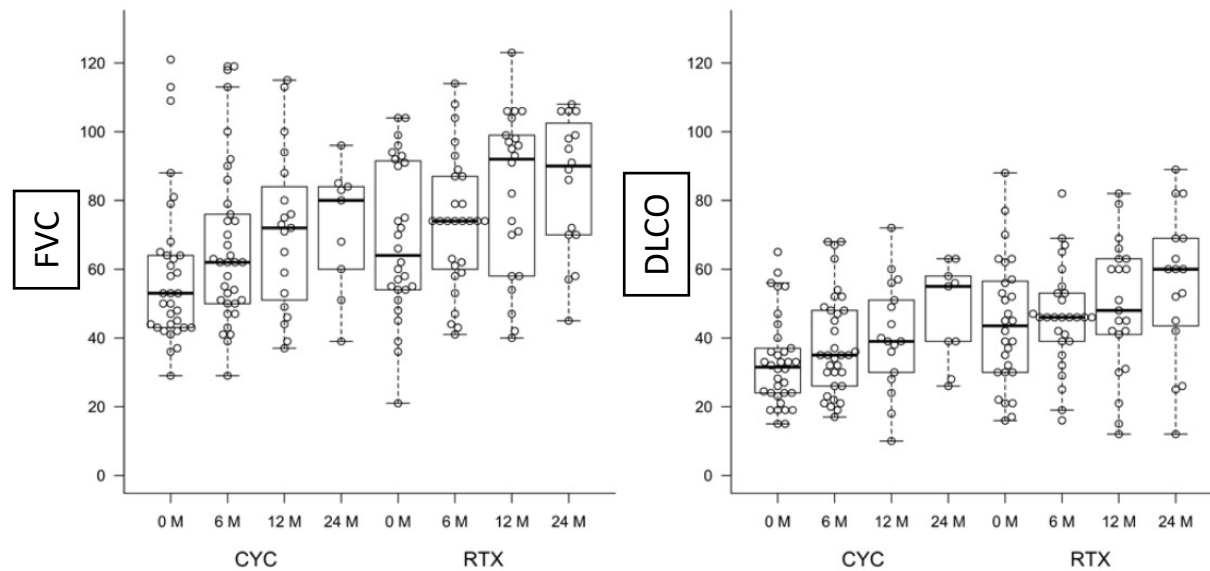
- All had an NSIP pattern of disease (CTD, IPAF, or idiopathic)
- MMF 2g daily + Rituximab/Placebo for 6 months
- 63 received RTX; 59 received placebo



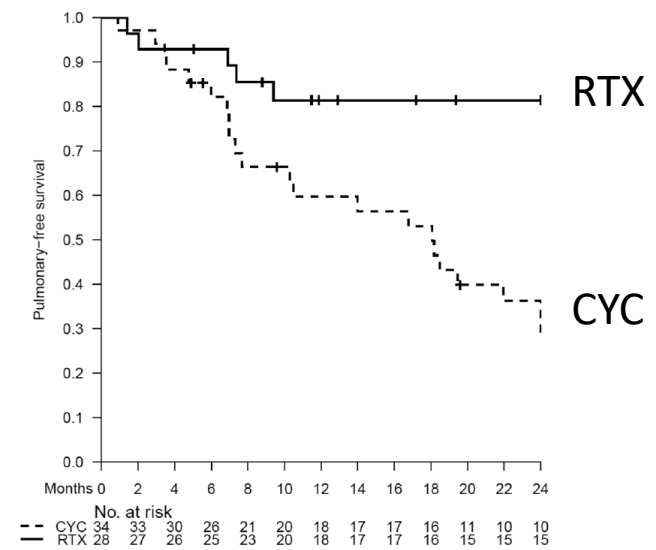
# RTX vs CYC for antisynthetase associated-ILD

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

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



Pulmonary-free survival



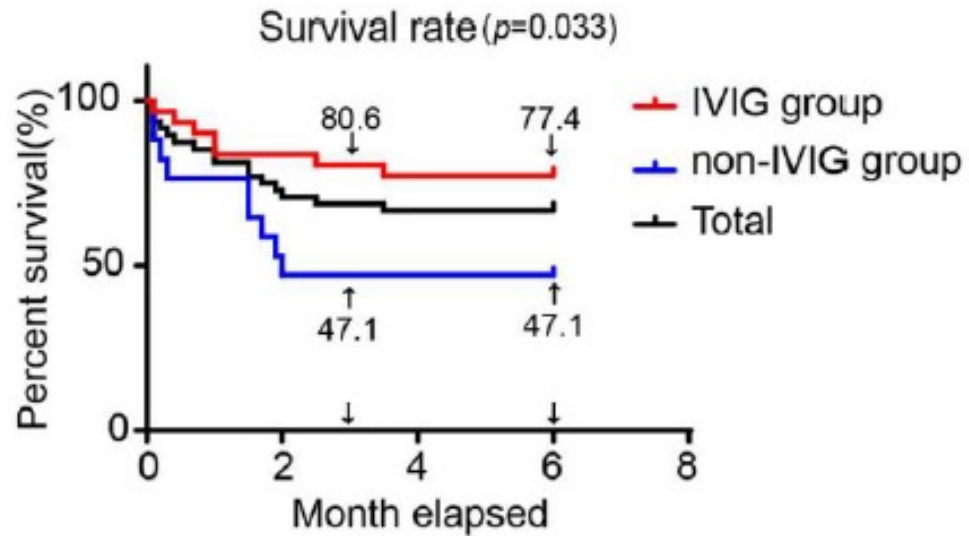
\*CYC has statistically significant lower FVC and DLCO at baseline

# 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:

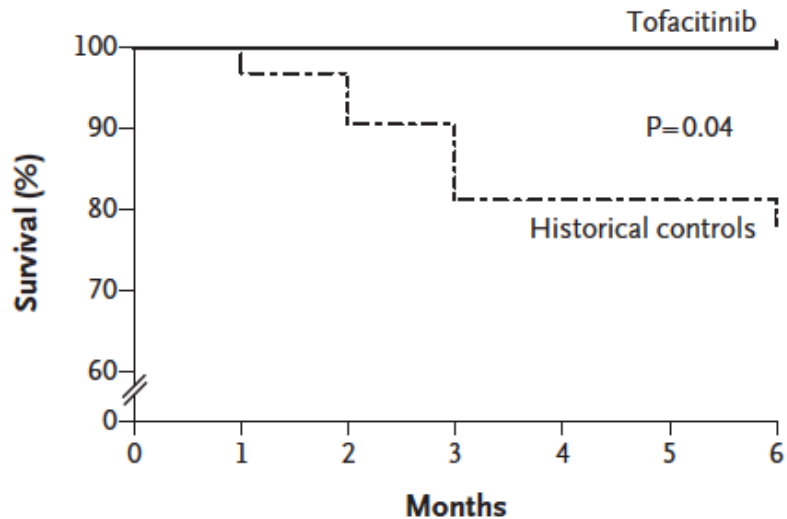
IVIg 71%

Standard therapy 41.2%  $p = 0.044$

# Tofacitinib for MDA5-ILD

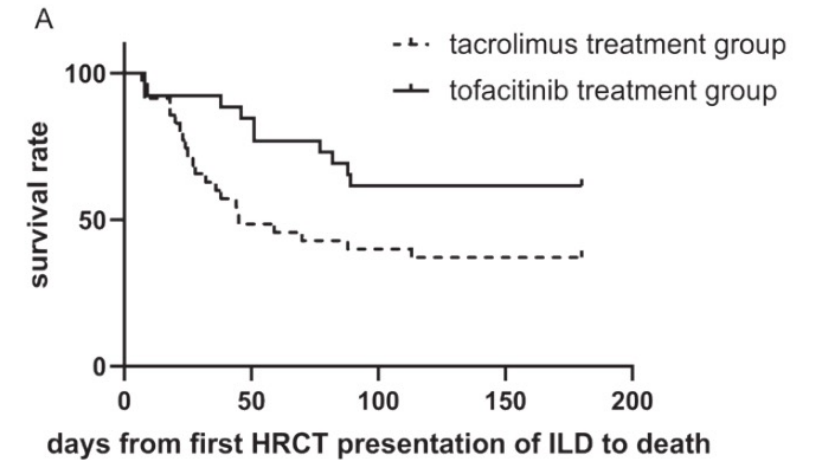
18 pts received Tofacitinib vs 32 historical controls

- 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%;  $P = 0.03$ )

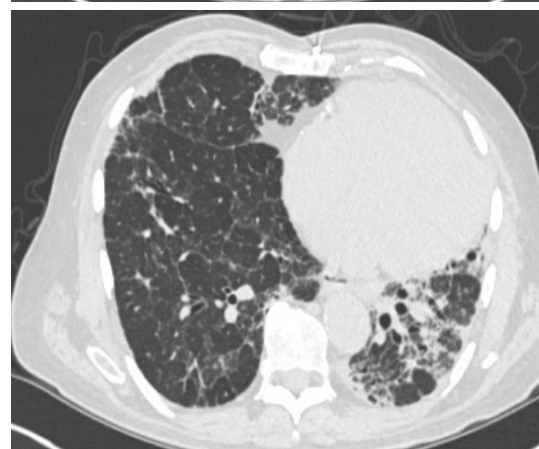
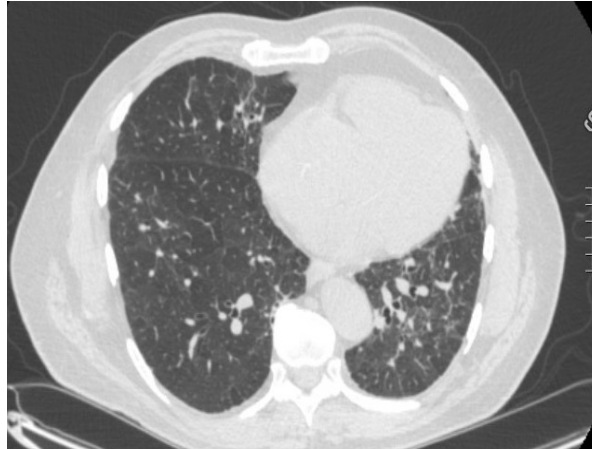
# Myositis patients can develop a progressive fibrotic phenotype

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

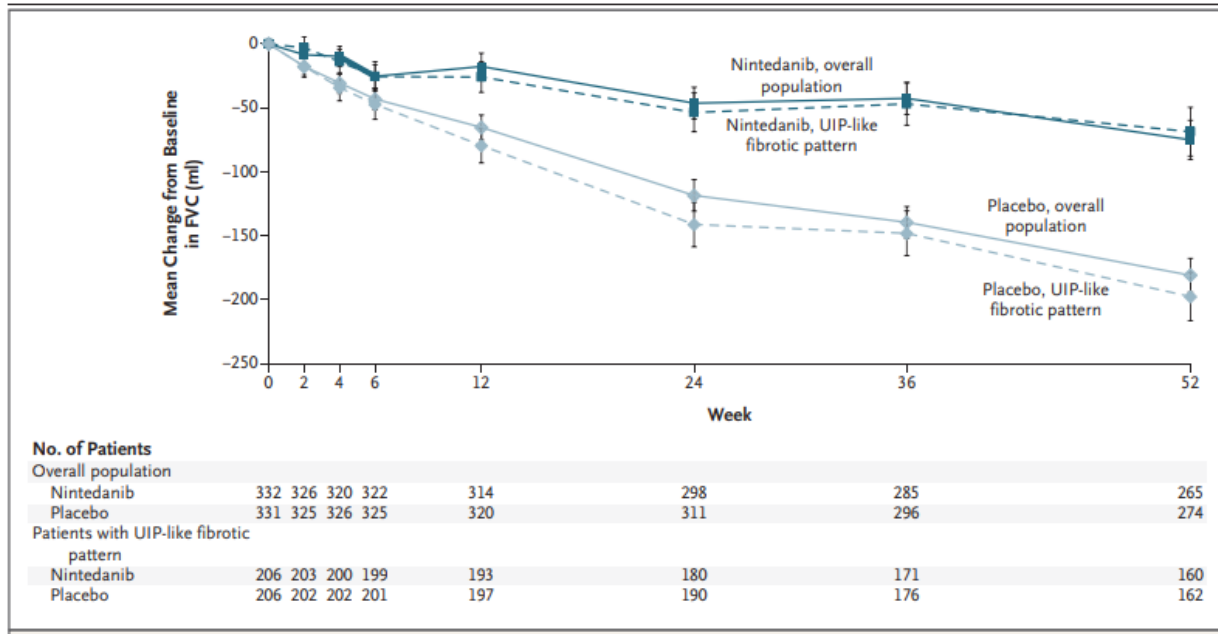
2019



2021



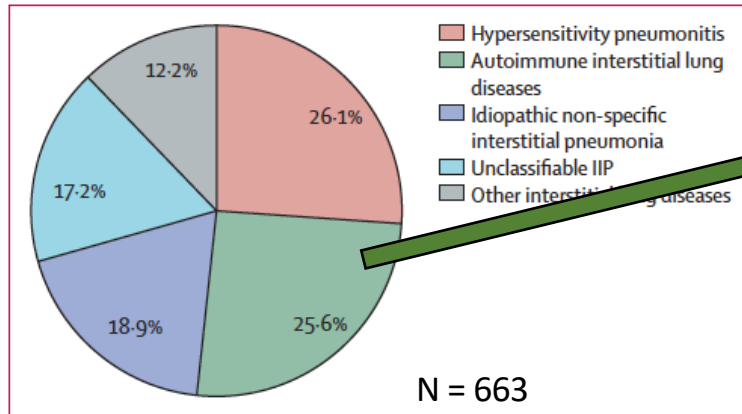
# INBUILD — Nintedanib is effective for patients with PF-ILD (non-IPF)



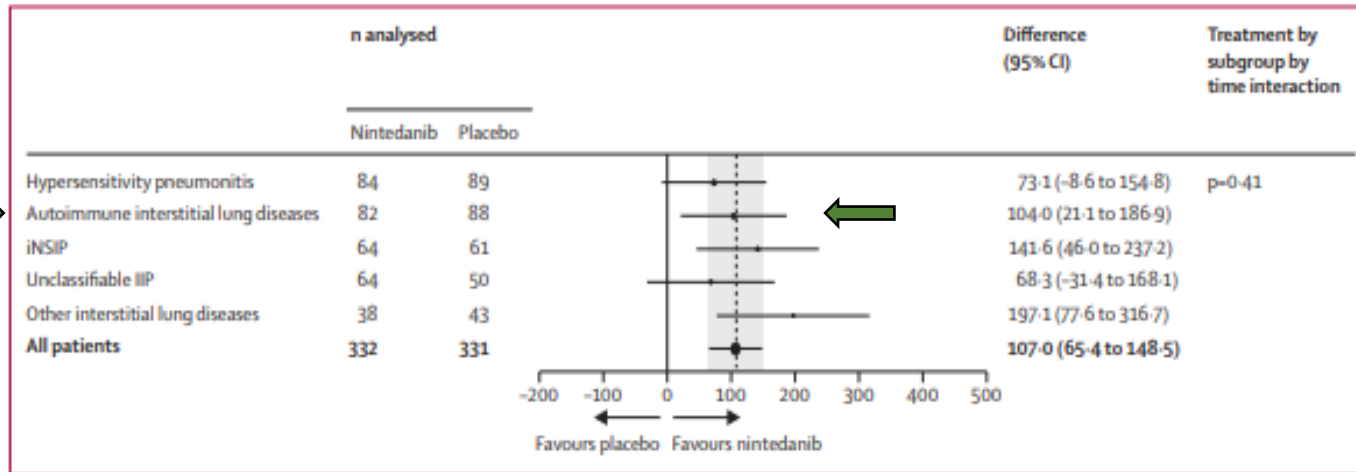
**Table 2. Efficacy End Points.\***

End Point	Nintedanib (N=332)	Placebo (N=331)	Difference (95% CI)
<b>Primary end point</b>			
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





# 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%

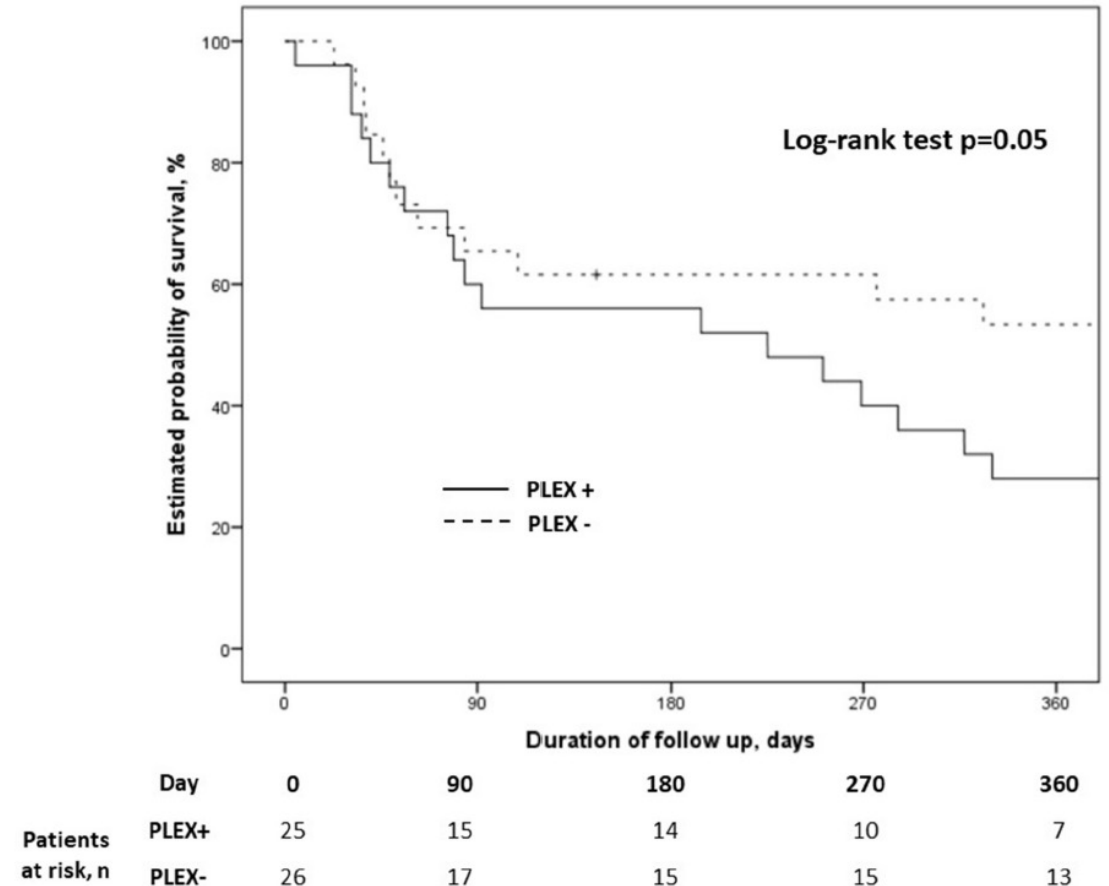
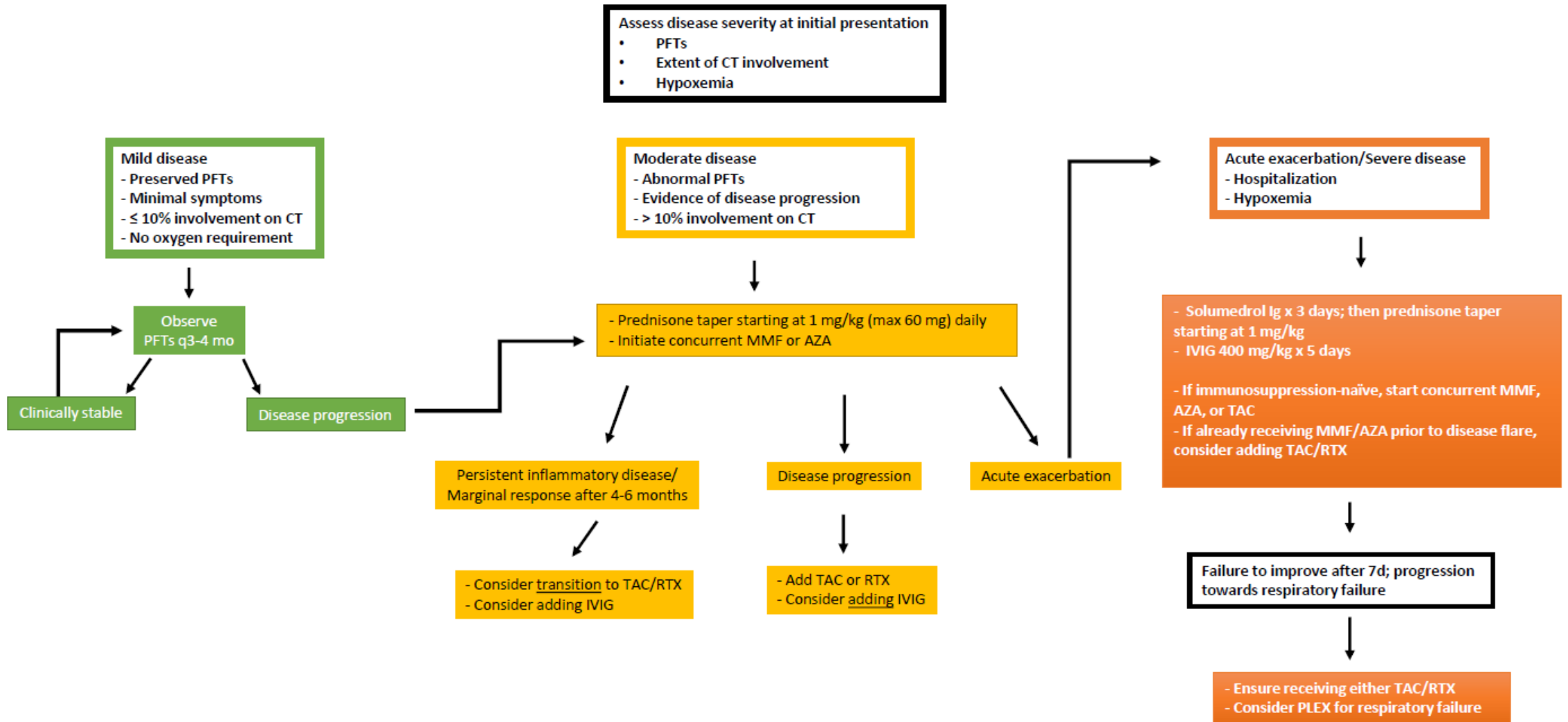


Fig. 2. Kaplan-Meier Curves for the One-Year Transplant-Free Survival According to the use of Plasma Exchange.

# Treatment algorithm



# Summary

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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

