

Myositis-associated ILD: update on treatment approaches and challenges

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Disclosures

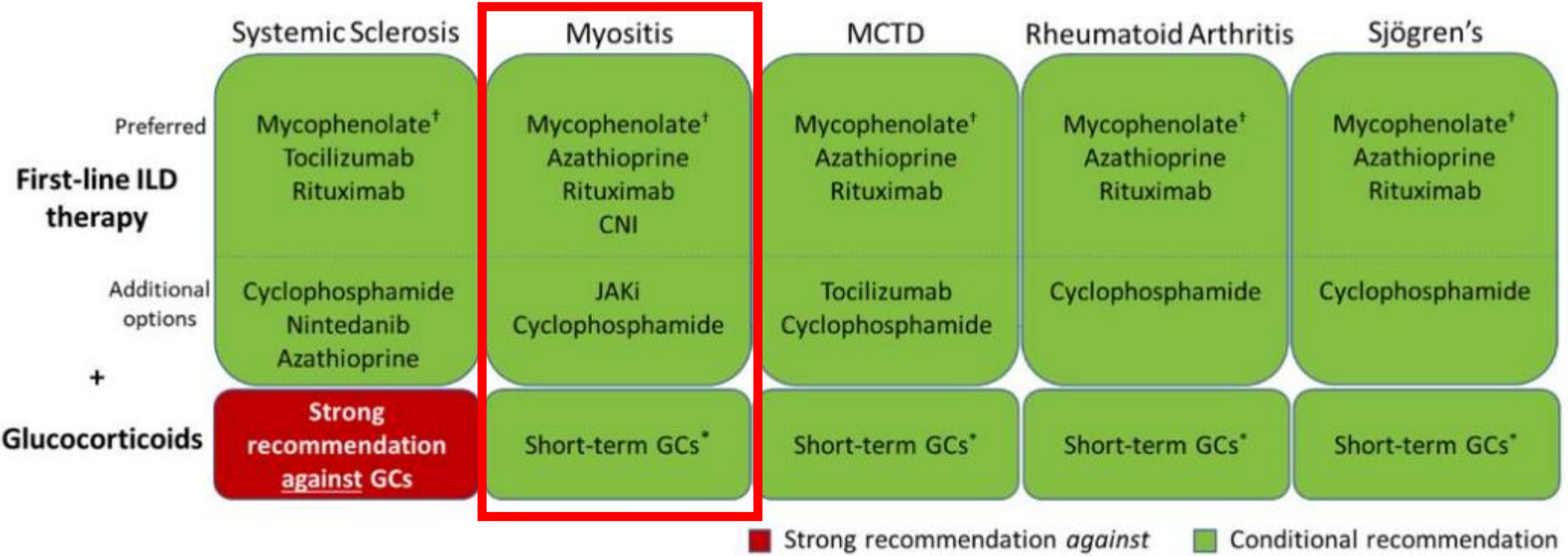
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- PI on clinical trials: Boehringer Ingelheim, Vicore



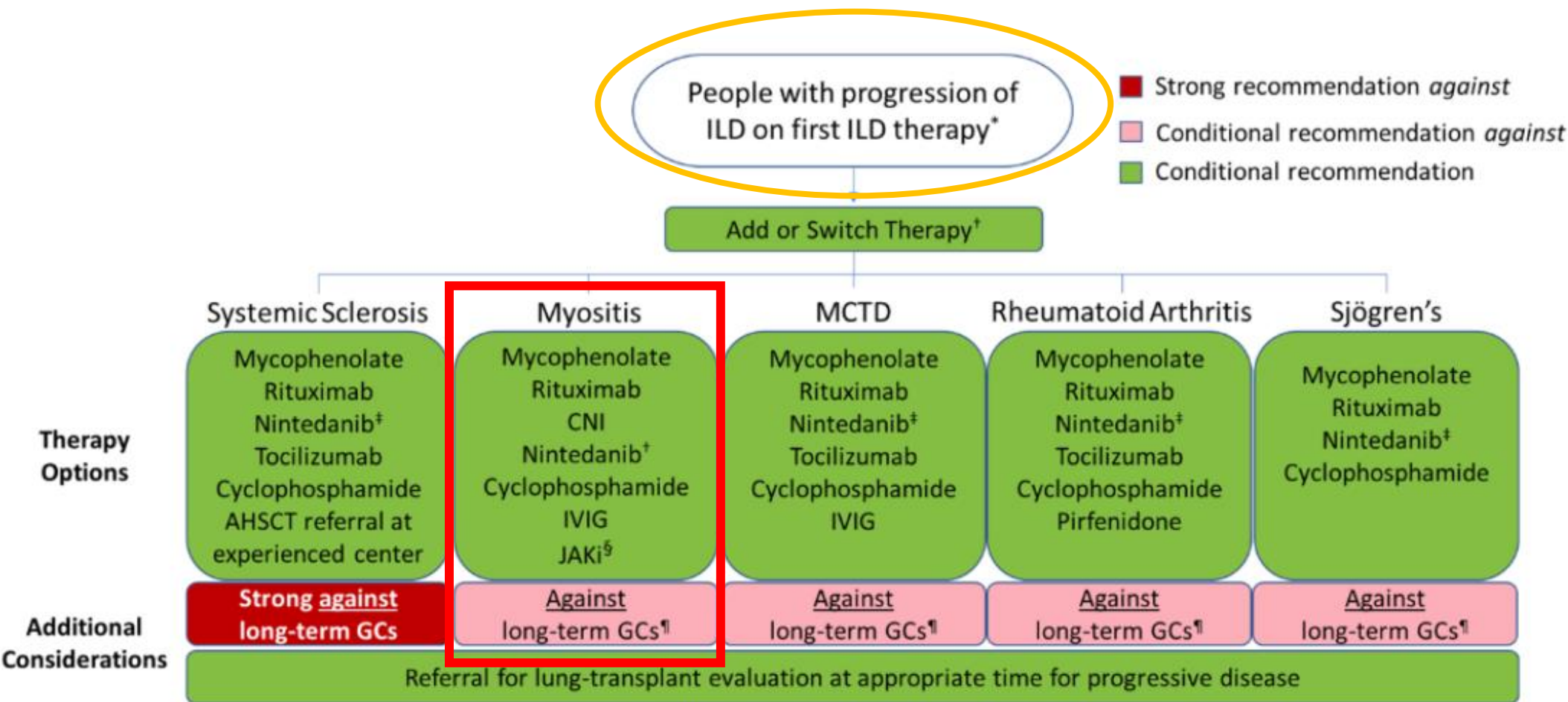
ILD is common in patients with myositis

- 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)



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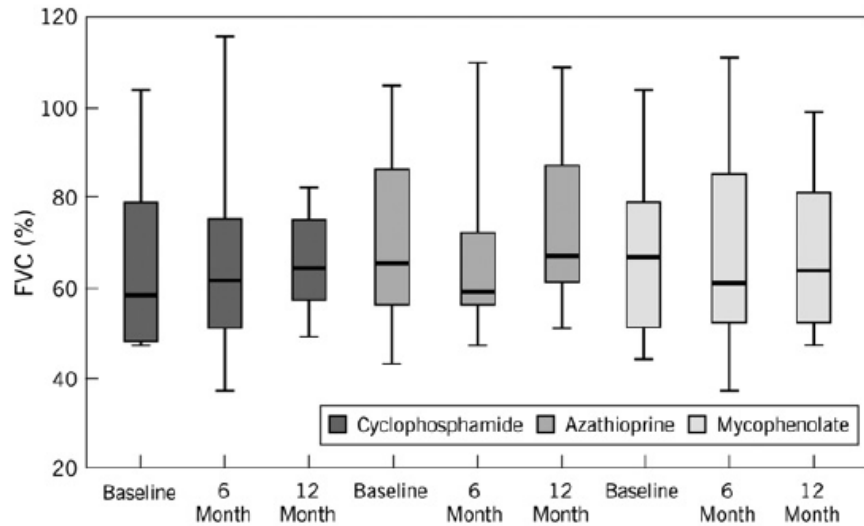
Myositis-ILD can be stabilized by a variety of agents

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

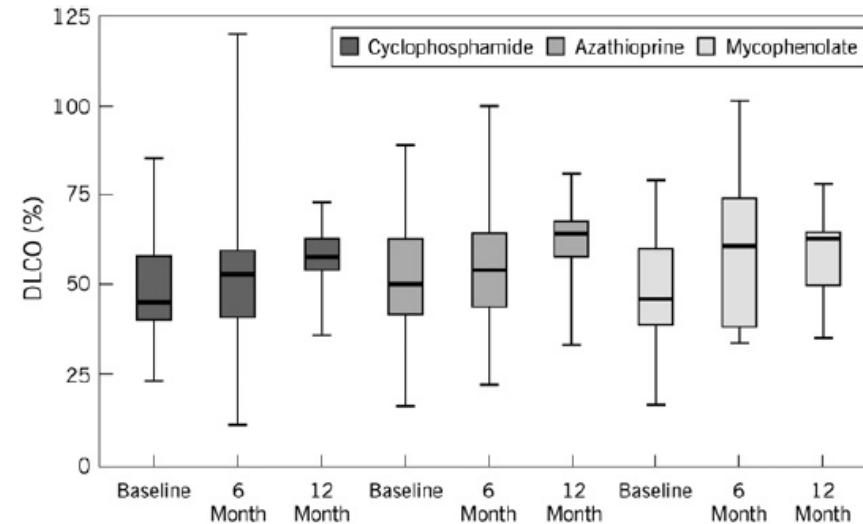
Cyclophosphamide 24

Azathioprine 13

Mycophenolate 9



FVC increased by 5%

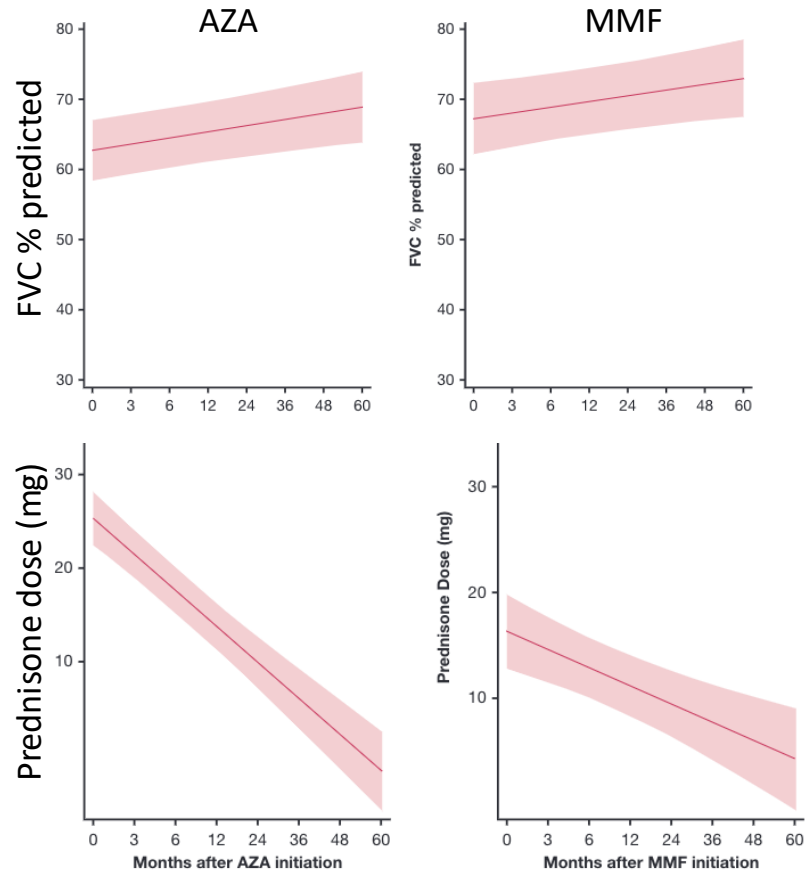


DLCO increased by 2.9%

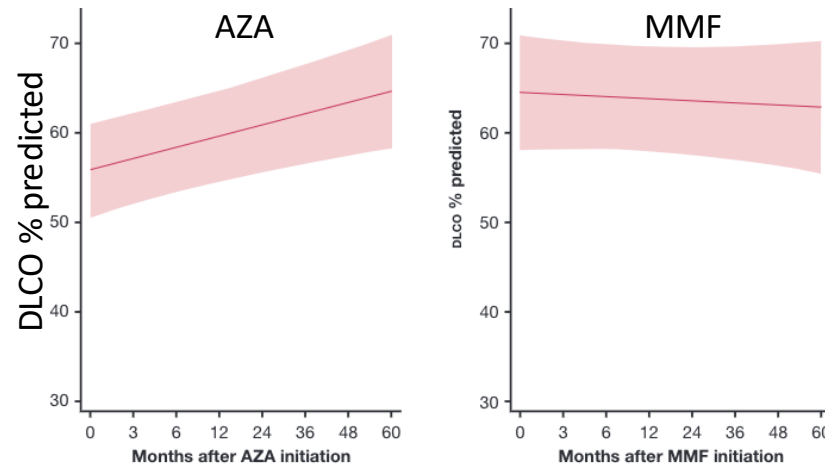
Ave prednisone dose: 40 mg/d pre-treatment; 10-16 mg/d at 6 months; 7.5 mg/d at 12 months



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%)



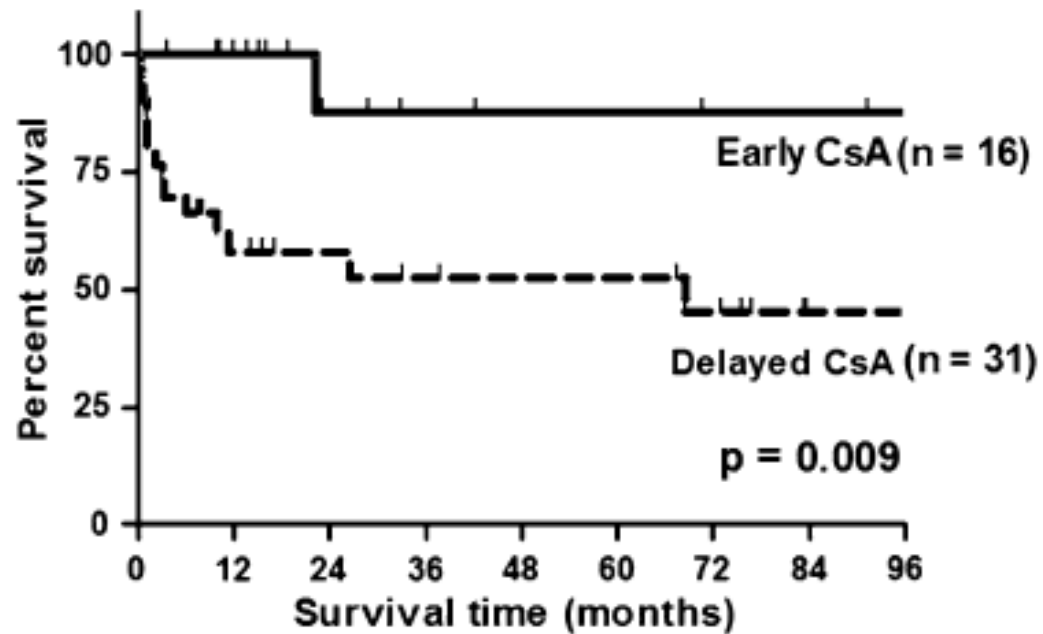
Early use of calcineurin inhibitors may be beneficial for myositis-ILD

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

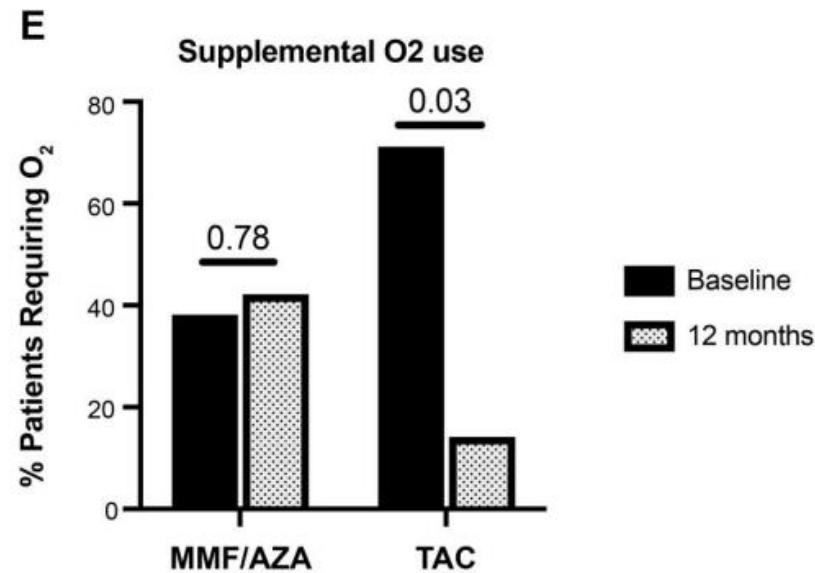
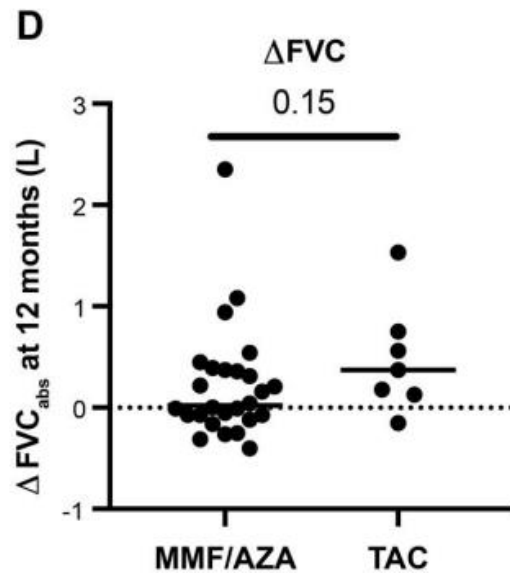
- Often received other steroid-sparing agents first



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

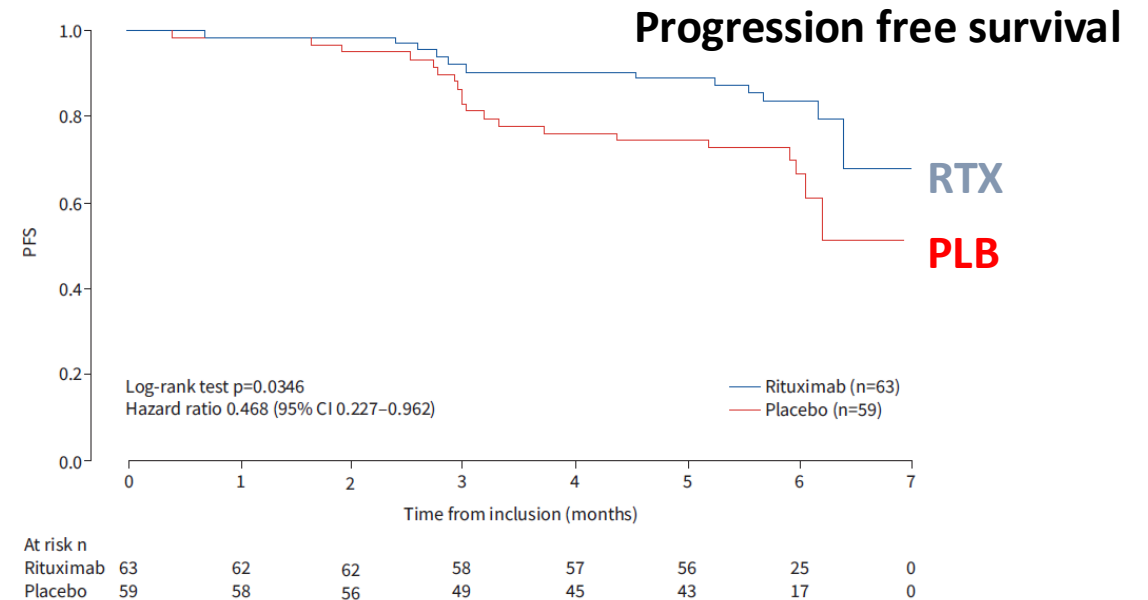
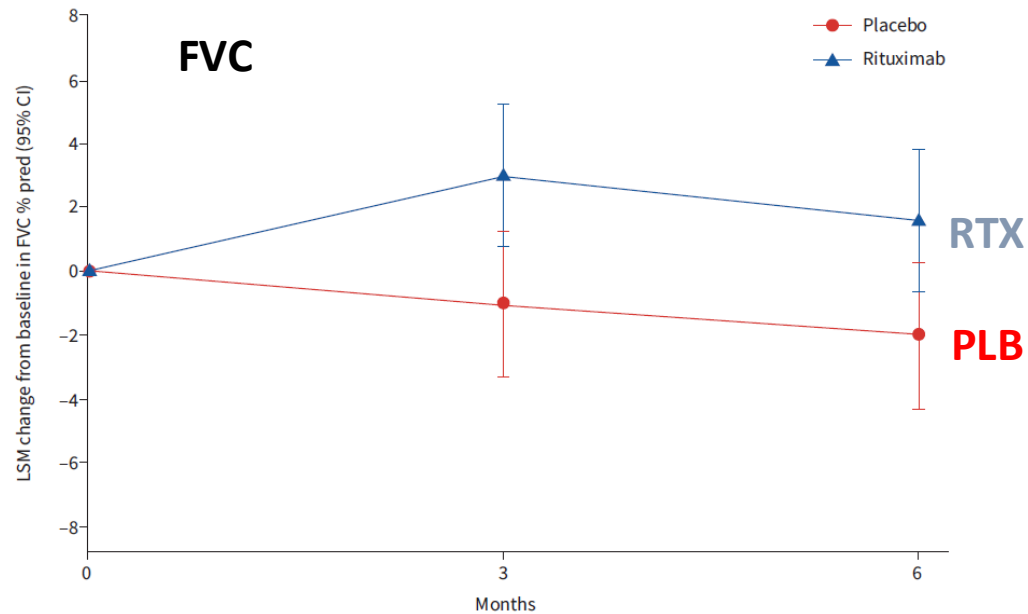
Tacrolimus is an effective first-line therapy in patients with myositis-ILD

- Retrospective cohort study of myositis-ILD patients followed 12 months
- *Steroid-sparing agent naïve*
- MMF/AZA = 26; TAC = 7
- MDA5 only represented in TAC group (5 vs 0)
- TAC group received more IVIG (43% vs 12%)



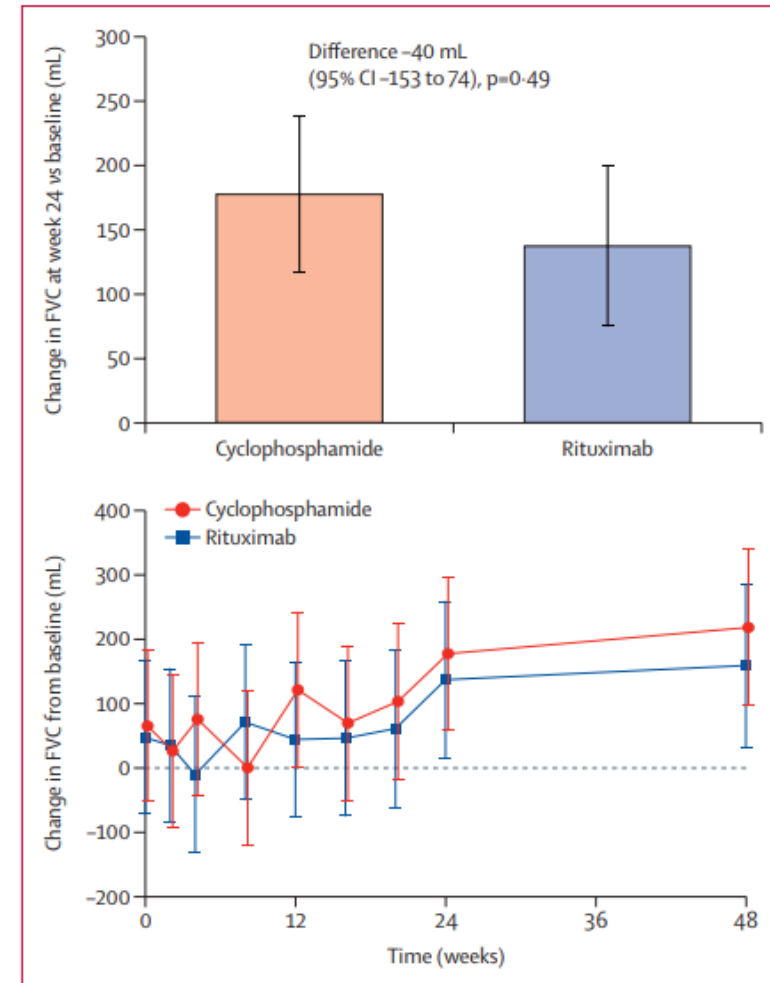
Rituximab and mycophenolate mofetil combination in patients with interstitial lung disease (EVER-ILD): a double-blind, randomized, placebo-controlled trial

- 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



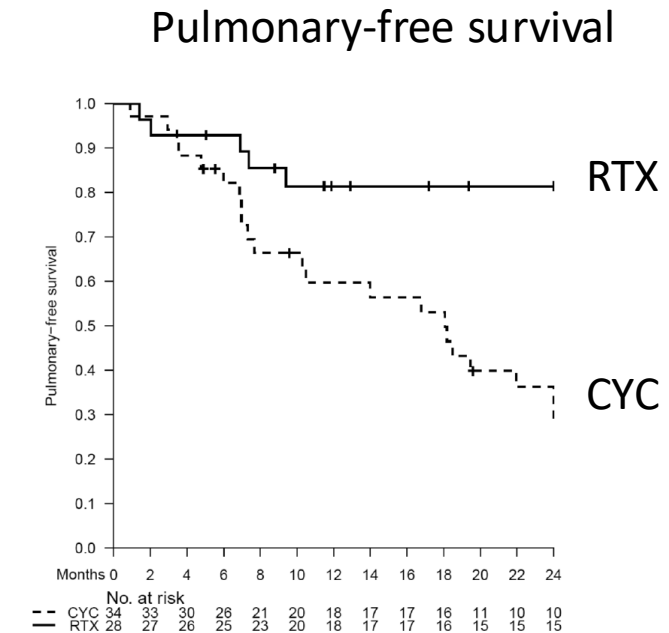
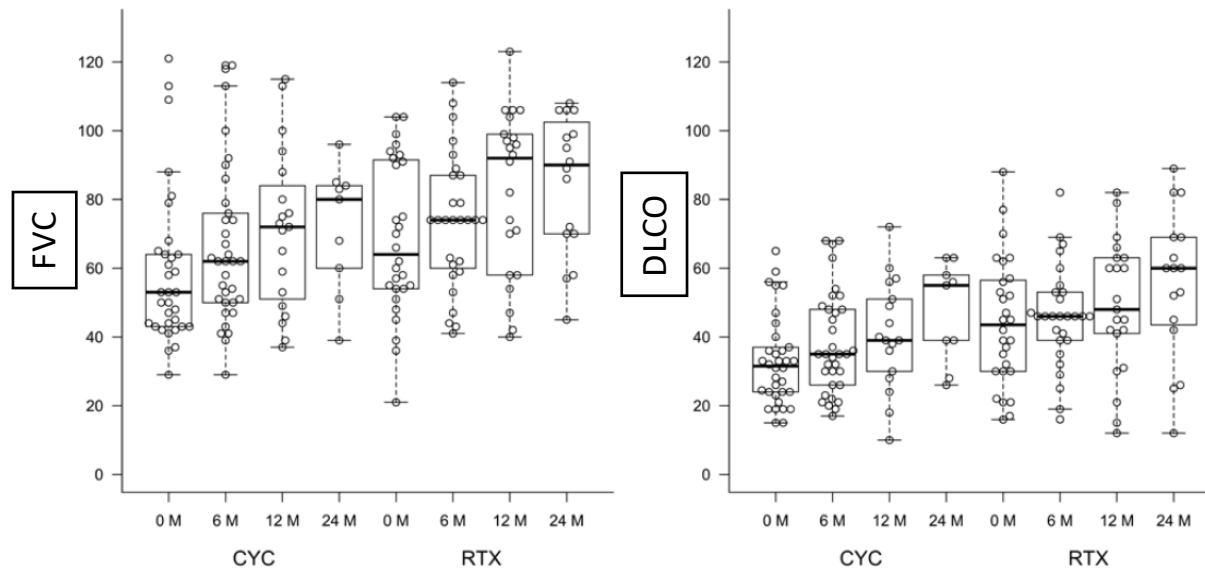
Rituximab vs Cyclophosphamide for progressive CTD-ILD (RECITAL)

- Phase II RCT in 11 UK centers
- 48 patients in CYC group; 49 in RTX group
 - **45.4% Myositis**
 - 38.1% Scleroderma
 - 16.5% MCTD
- No difference in FVC at either 24 or 48 weeks
- No difference in infection between groups



Is Rituximab superior to Cyclophosphamide in patients with anti-synthetase antibodies?

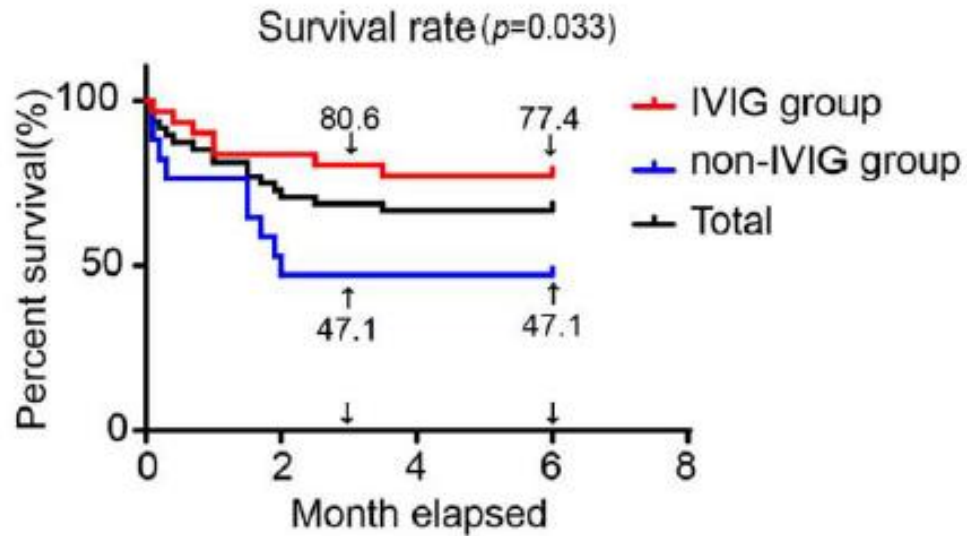
- CYC 34 patients (88% received subsequent steroid-sparing agents)
- RTX 28 patients (54% received subsequent steroid-sparing agents)



*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



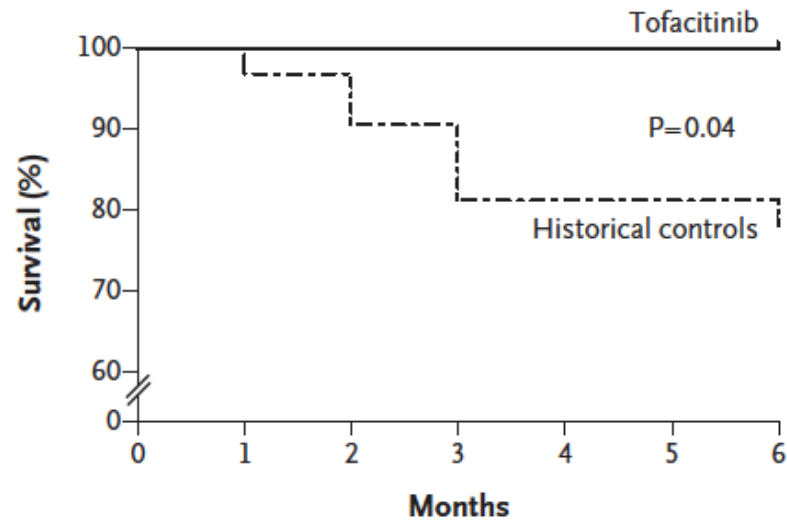
Remission rate at 3 months:

- IVIG 71%
- Standard therapy 41.2%
($p = 0.044$)

Tofacitinib for MDA5-ILD

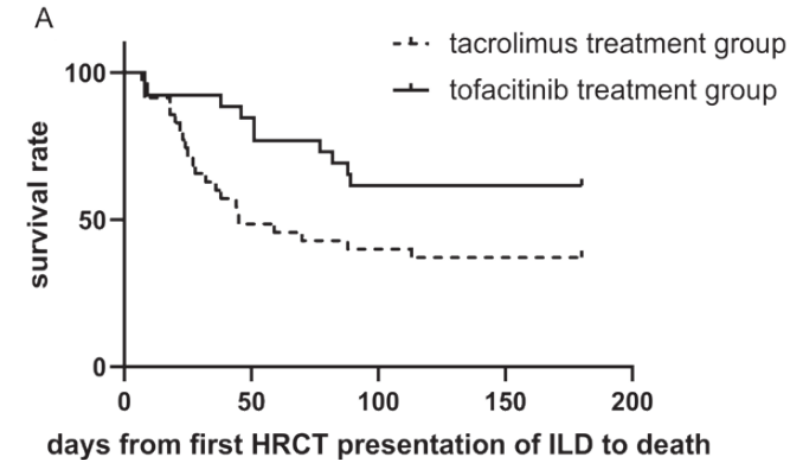
18 pts received Tofacitinib vs 32 historical controls

- ILD present less than 3 months
- Well matched for disease severity



26 patients received TOF; 35 received TAC

- Groups were relatively well matched
- More anti-Ro52 in TOF group
- More high-titer anti-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%; $P = 0.03$)

JAKi to treat anti-synthetase associated ILD

- Retrospective study of patients with anti-synthetase syndrome and ILD
- Received glucocorticoids and at least one steroid-sparing agent

Table 1

Patients' characteristics and treatment responses at baseline and after treatment.

#	Sex	Age	Myositis-specific antibody	Previous treatment	JAKi type	MMT8		VAS		CK		Infection	Prognosis
						before	after	before	after	before	after		
1	M	57	PL12	GC, HCQ, MMF	Baricitinib→Tofacitinib	78	80	9	7	34	66	COVID-19	Remission
2	M	56	PL7	GC, CYC	Baricitinib	80	80	6	0	139	88	CMV	Remission
3	F	33	PL7	GC, CsA, TAC, HCQ, Thd	Baricitinib	71	79	8	1	258	47		Remission
4	M	51	Jo-1	GC, HCQ	Baricitinib	80	NA	4	NA	149	NA	COVID-19	Death
5	M	58	PL7	GC, CsA, MMF, TCZ	Tofacitinib	80	80	8	8	45	44	MTB	Stable
6	F	32	PL7	GC, Thd, MMF	Baricitinib	75	78	8	2	2880	163		Remission
7	F	41	PL7	GC, HCQ, MMF, CsA	Tofacitinib	80	80	1	0	18	56	CMV	Remission
8	M	34	Jo-1	GC, CsA, MTX	Tofacitinib	58	80	9	0	107	50	MTB	Remission
9	M	61	PL7	GC, CYC, CsA	Tofacitinib	72	80	8	5	94	NA		Remission
10	F	46	OJ	GC, TAC	Tofacitinib	80	80	4	0	74	NA		Remission
11	F	53	Jo-1	GC, MTX, LEF, CYC	Tofacitinib→Baricitinib	80	80	8	0	915	92		Remission
12	F	56	Jo-1	GC, CYC, IVIG, CsA, MMF	Tofacitinib	77	77	4	1	30	45	Skin	Stable
13	M	54	PL12	GC, TAC	Tofacitinib	80	80	3	0	128	130		Remission
14	M	66	PL7	GC, CYC	Tofacitinib	80	80	6	0	157	78		Remission
15	M	56	PL7	GC, IVIG, MMF, CYC	Tofacitinib	80	NA	8	NA	63	900	CMV	Death
16	F	58	PL7	GC, TAC	Tofacitinib	78	78	6	2	70	110		Remission
17	F	59	Jo-1	GC, HCQ, CsA	Tofacitinib	80	NA	6	3	52	NA		Stable
18	F	49	Jo-1	GC, MMF, TAC	Tofacitinib	80	80	8	0	29	64	Urinary tract	Remission
19	F	34	EJ	GC, AZA, MMF, IGU, TAC, Thd, MTX	Tofacitinib	80	80	1	3	979	302	CMV	Stable
20	M	72	EJ	GC, IVIG, CsA	Tofacitinib	80	80	8	5	448	392		Remission

JAKi to treat anti-synthetase associated ILD

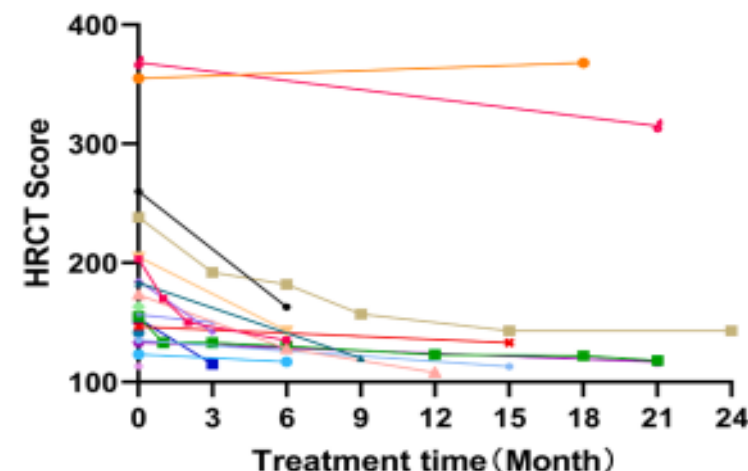


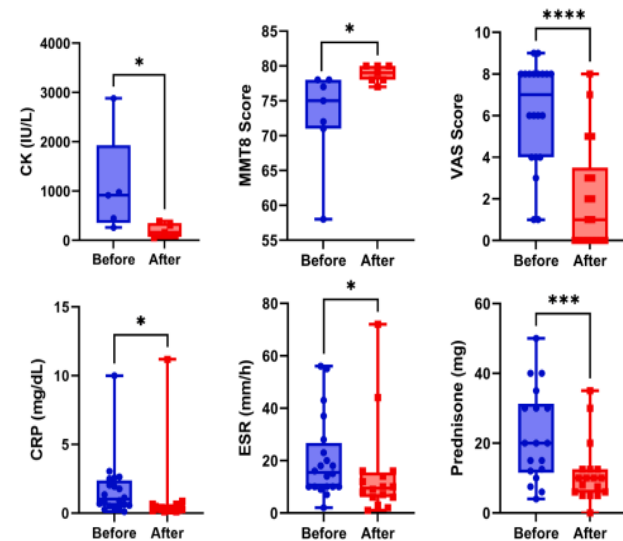
Table 2

Comparison of clinical features before and after treatment.

	Baseline	After treatment	p
Fever	6 (33.3 %)	1 (5.6 %)	0.063
Periorbital edema	7 (38.9 %)	2 (11.1 %)	0.063
Arthritis	11 (61.1 %)	1 (5.6 %)	0.002**
Skin rash	14 (77.8 %)	5 (27.8 %)	0.012*
Mechanic hand	11 (61.1 %)	5 (27.8 %)	0.07
Shortness of breath	10 (55.6 %)	3 (16.7 %)	0.039*
Cough	11 (61.1 %)	2 (11.1 %)	0.012*
Myositis	9 (50 %)	2 (11.1 %)	0.016*
Fatigue	11 (61.1 %)	2 (11.1 %)	0.012*

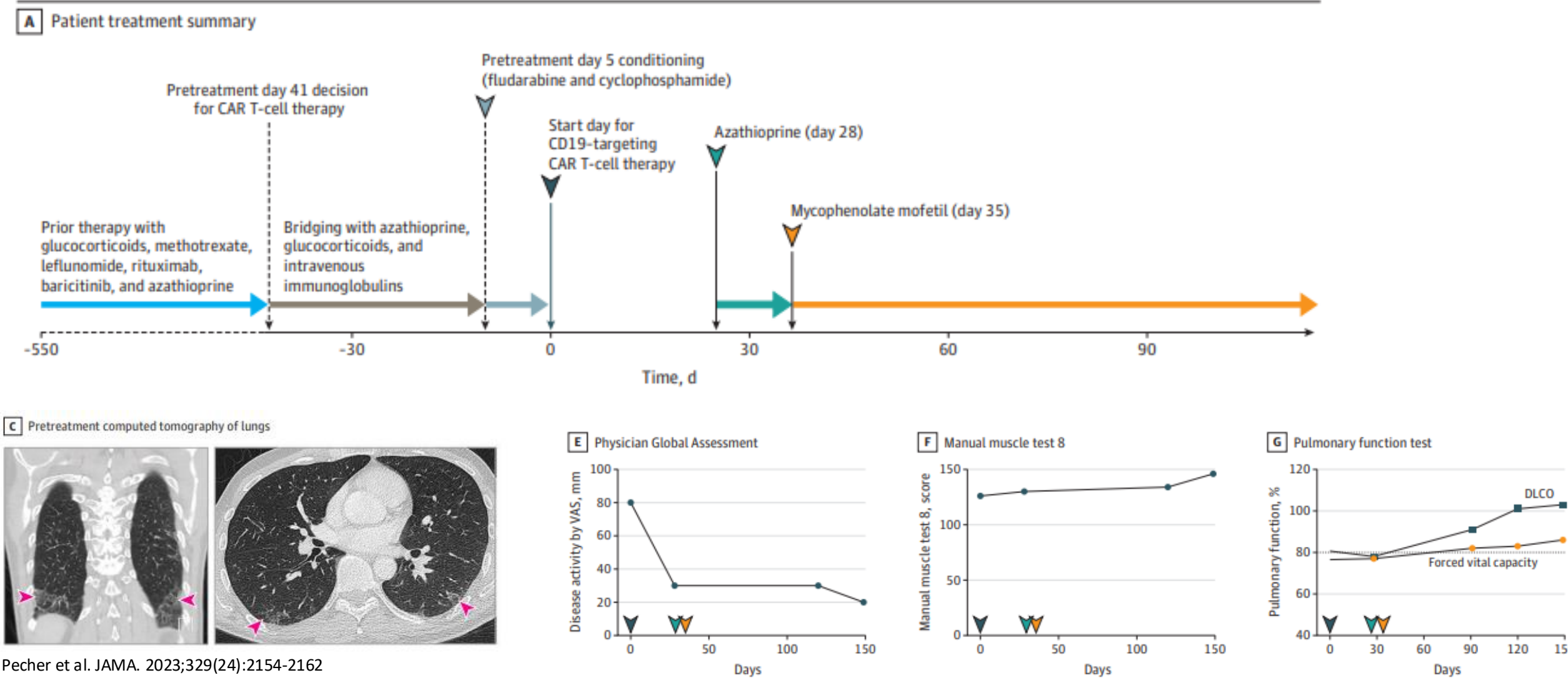
* $p < 0.05$.

** $p < 0.01$.



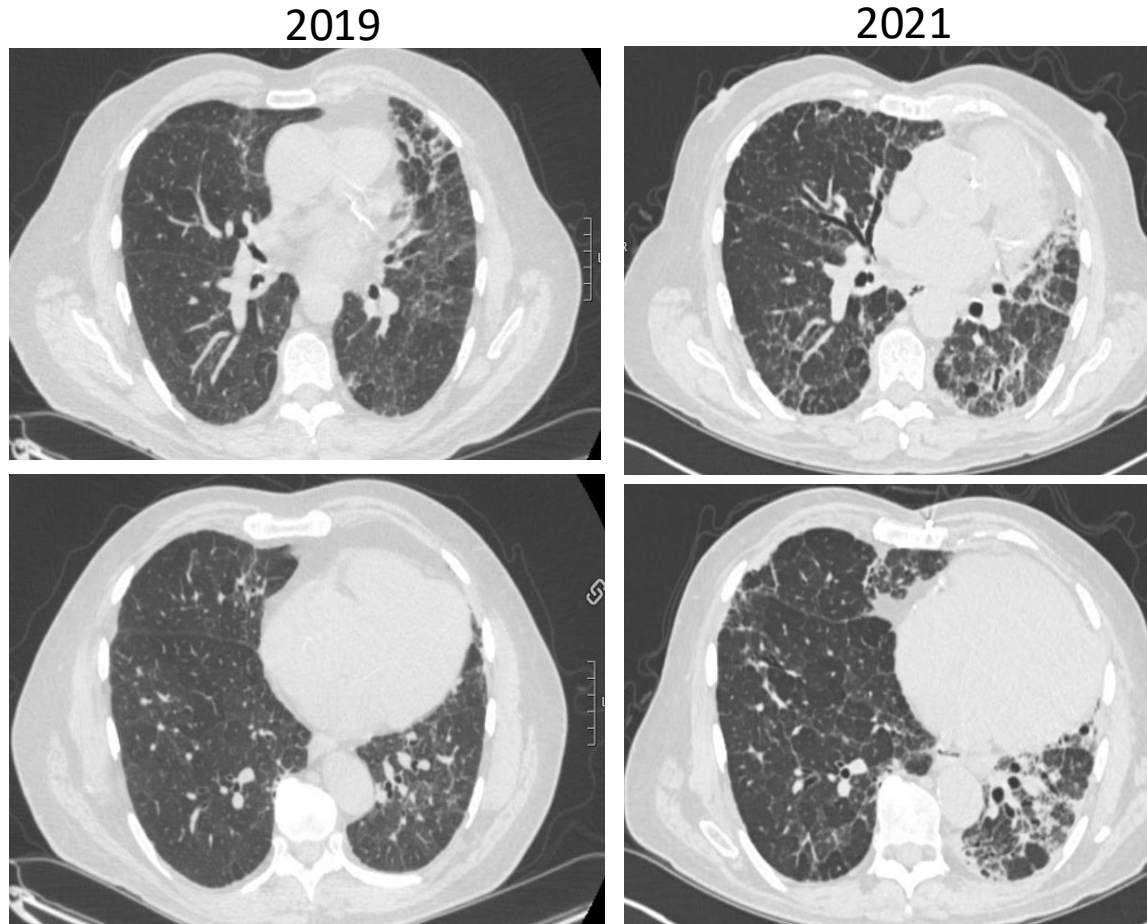
CD19-Targeting CAR T Cells for Myositis and Interstitial Lung Disease Associated With Antisynthetase Syndrome

Figure 1. Patient's Clinical Details and Treatment History



Myositis patients can develop a progressive fibrotic phenotype

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



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

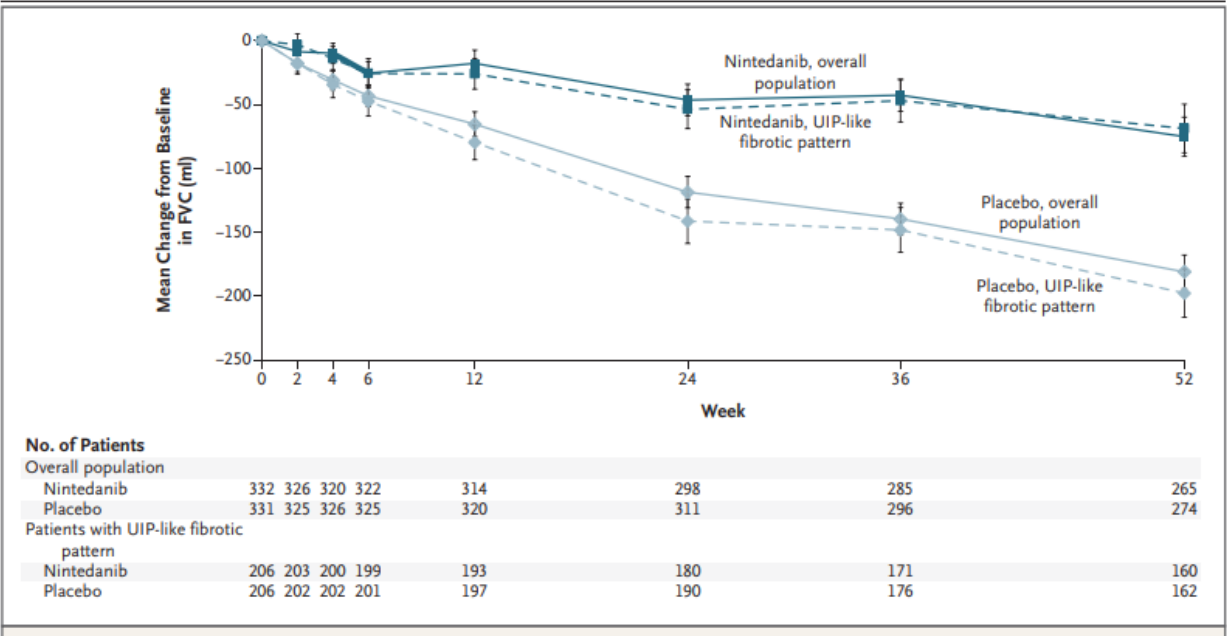
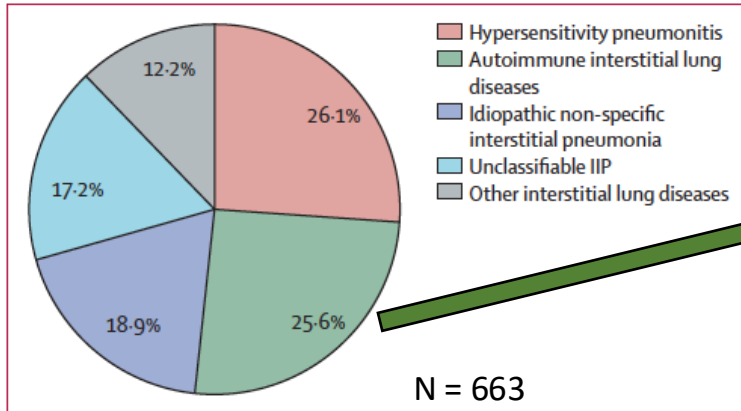


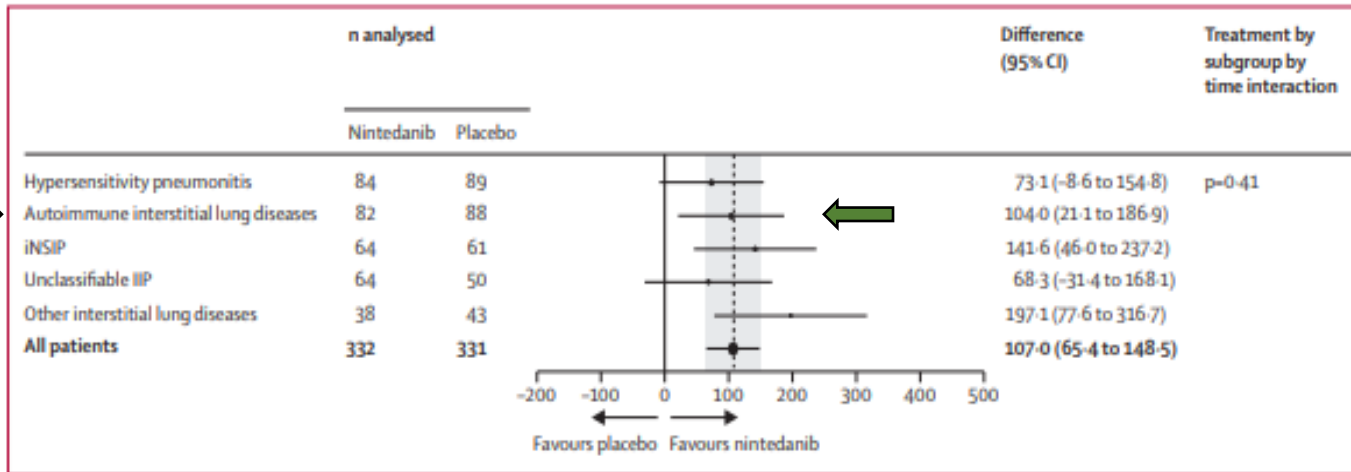
Table 2. Efficacy End Points.*			
End Point	Nintedanib (N=332)	Placebo (N=331)	Difference (95% CI)
Primary end point			
Rate of decline in the FVC at 52 wk — ml/yr†			
Overall population	−80.8±15.1	−187.8±14.8	107.0 (65.4 to 148.5)‡
Patients with a UIP-like fibrotic pattern	−82.9±20.8	−211.1±20.5	128.2 (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



The Fibroneer study (Nerandomilast) also did not evaluate patients with myositis

ILD diagnoses

Table S1. ILD diagnoses as per the categories in the case report form*

	Placebo (N = 392)	Nerandomilast 9 mg twice daily (N = 393)	Nerandomilast 18 mg twice daily (N = 391)
Hypersensitivity pneumonitis	77 (19.6)	83 (21.1)	73 (18.7)
Unclassifiable idiopathic interstitial pneumonia	82 (20.9)	76 (19.3)	73 (18.7)
Idiopathic non-specific interstitial pneumonia	73 (18.6)	73 (18.6)	82 (21.0)
Rheumatoid arthritis-associated ILD	32 (8.2)	45 (11.5)	41 (10.5)
Systemic sclerosis-associated ILD	23 (5.9)	25 (6.4)	27 (6.9)
Mixed connective tissue disease-associated ILD	12 (3.1)	16 (4.1)	19 (4.9)
Exposure-related ILD	12 (3.1)	11 (2.8)	9 (2.3)
Sarcoidosis-ILD	8 (2.0)	6 (1.5)	3 (0.8)
Other fibrosing ILDs	73 (18.6)	58 (14.8)	64 (16.4)

*Data are no. (%).

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%

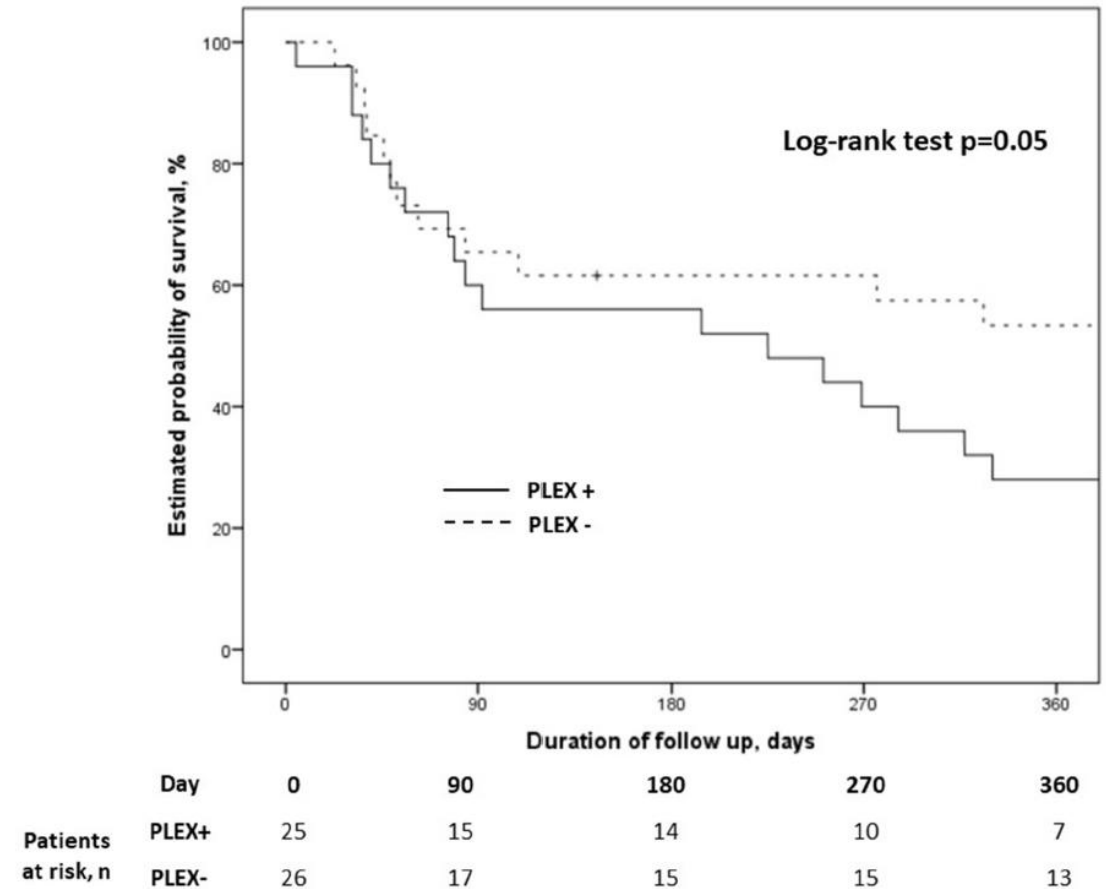
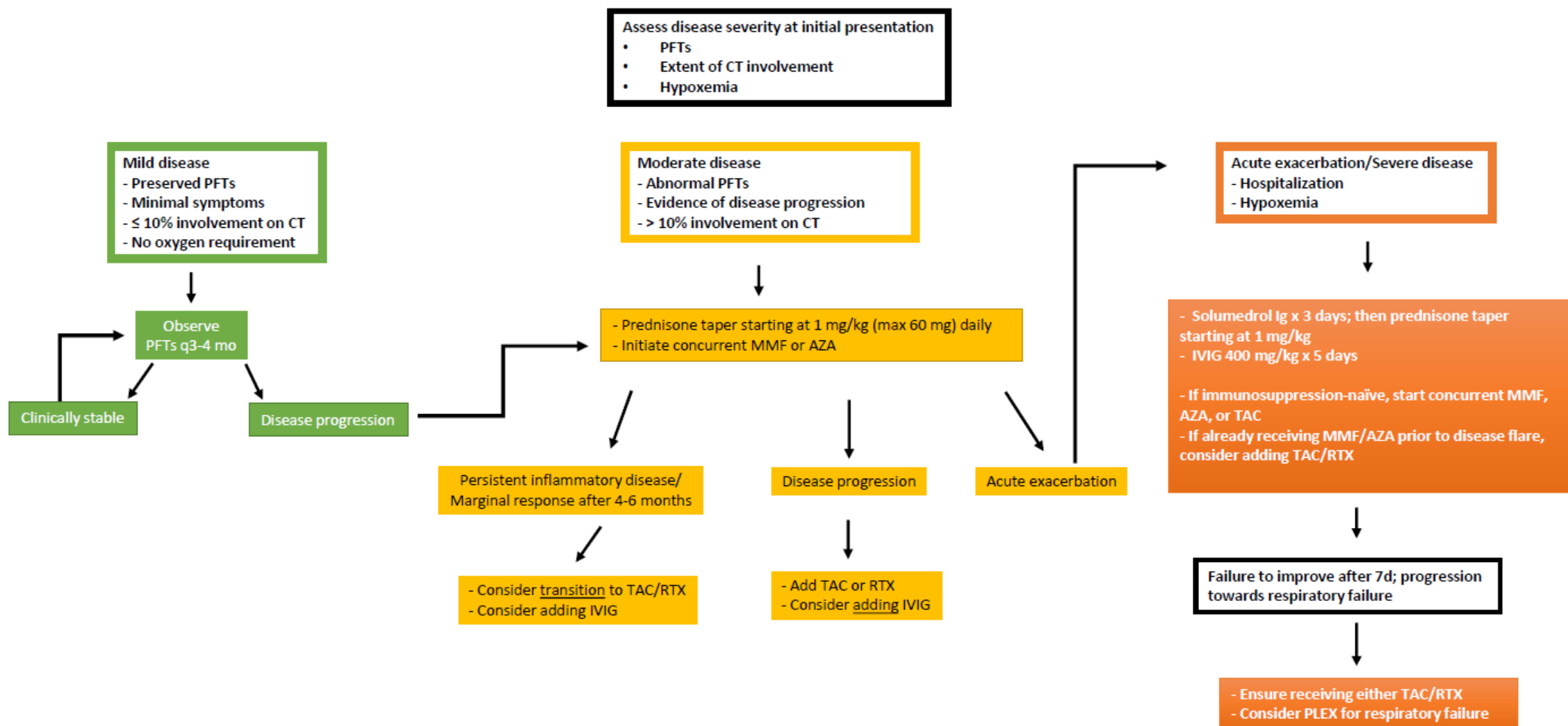


Fig. 2. Kaplan-Meier Curves for the One-Year Transplant-Free Survival According to the use of Plasma Exchange.

Treatment algorithm



Summary

- 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

