# CTD-ILD
# : A Practical Guide for Pulmonologists

2026. 07. 4

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# Case 1 (F/48)

Myalgia, periorbital swelling, rash, cough, sputum

Dyspnea, fever

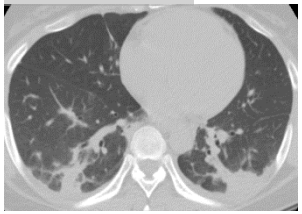
Dyspnea, fever, Well-being sense(-)

2025. 2.10(ER)

2025. 2.13(Adm)~2.28

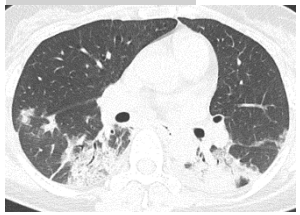
2025. 3.5(Adm)~5.2

2025. 2.10



Antibiotics

2025. 2.17

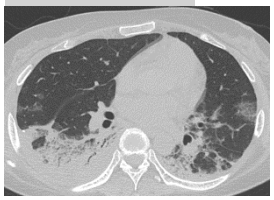


R/A: 96% (2.13)

AST/ALT 246/82
CPK 409, Aldolase 28, LDH 474
FANA(+),
SSA/B(+/+)
Jo-1(-), EMG(+)

VATS Bx(2.21)
: OP pattern
➔ Steroid 1mg/kg

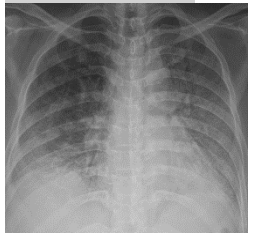
2025. 3.21



NP 1L : 94%
MDA 5 (+)

Steroid IV 1mg/kg
+ Azathioprine (3.5~)
⇒ Steroid pulse(3.21-23)
⇒ Rituximab
(비급여, 3.27)
➔ M enz & CXR 호전

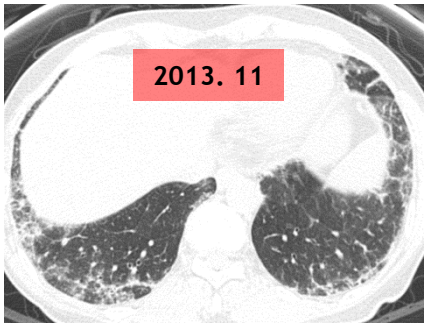
2025. 4.3



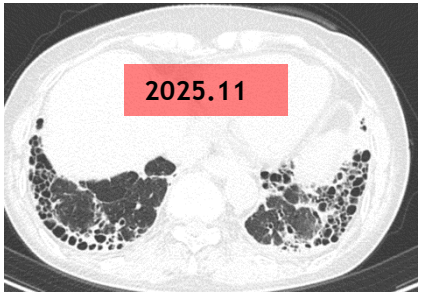
CXR 악화
Optiflow apply (4.3)
➔ PCP 의심하여
ICU 전실, intubation
PCP 치료 (4.4~)
➔ 호전 중 다시 악화
ECMO apply (4.9~)
➔ CMV 치료 (4.11~)
➔ Lung transplantation

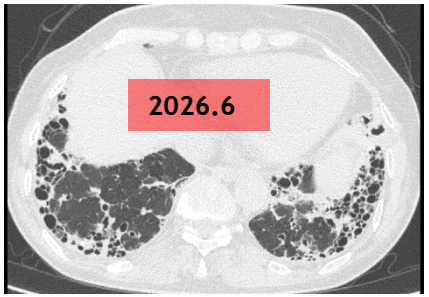
# Case 2 (F/73)

- 2013년 기침, 가래, 호흡곤란
  및 Chest CT에서 ILD 의심되어 내원
  ➔ VATS lung Bx(2013. 11)에서 NSIP pattern
  ➔ Sjögren's dz 진단, steroid 치료 후 f/u 중




| | FVC(%) | $DL_{CO}$ (%) |
|---|---|---|
| 2020.6 | 88 | 45 |
| 2023.9 | 81 | 43 |
| 2024.12 | 71 | 37 |
| 2025.11 | 59 | 38 |
| 2026.2 | 55 | 33 |
| 2026.6 | 70 | 40 |




Microscopic hematuria로 본원 신장내과에서 GN W/U 시행
➔ Kd Bx (2025.7)
: pauci-immune ANCA GN (microscopic polyarteritis)
➔ Steroid start (2025.8~)
➔ Proteinuria 증가
➔ Rituximab, 2025.11 (2회) 시행

# Introduction

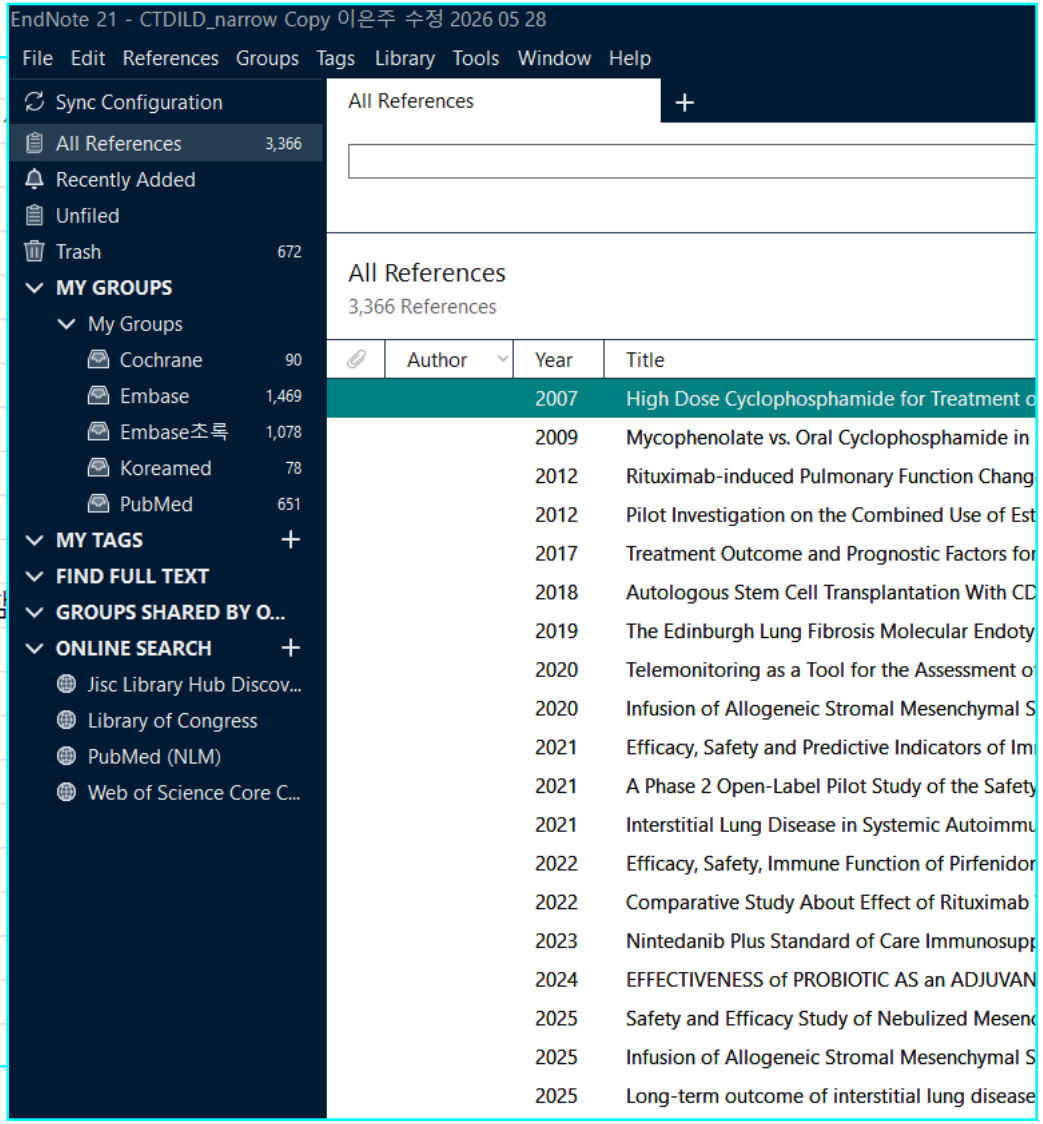
**검색일자: 2026. 5. 27.**

1. Broad search: 약물치료, 검사 및 평가 중 한 개 이

| 검색 DB | 검색건수 |
|---|---|
| PubMed | 4,781 |
| Embase | 19,775 |
| Cochrane Library | 608 |
| Koreamed | 120 |
| 전체 건수 | 5,509 |
| 중복 건수 | 110 |
| 최종 건수 | **5,399** |

2. Focused search: 약물치료, 검사 및 평가 모두 포함

| 검색 DB | 검색건수 |
|---|---|
| PubMed | 851 |
| Embase | 2,002 |
| Embase 초록 | 1,340 |
| Cochrane Library | 172 |
| Koreamed | 120 |
| 전체 건수 | 4,485 |
| 중복 건수 | 447 |
| 최종 건수 | **4,038** |



# Introduction

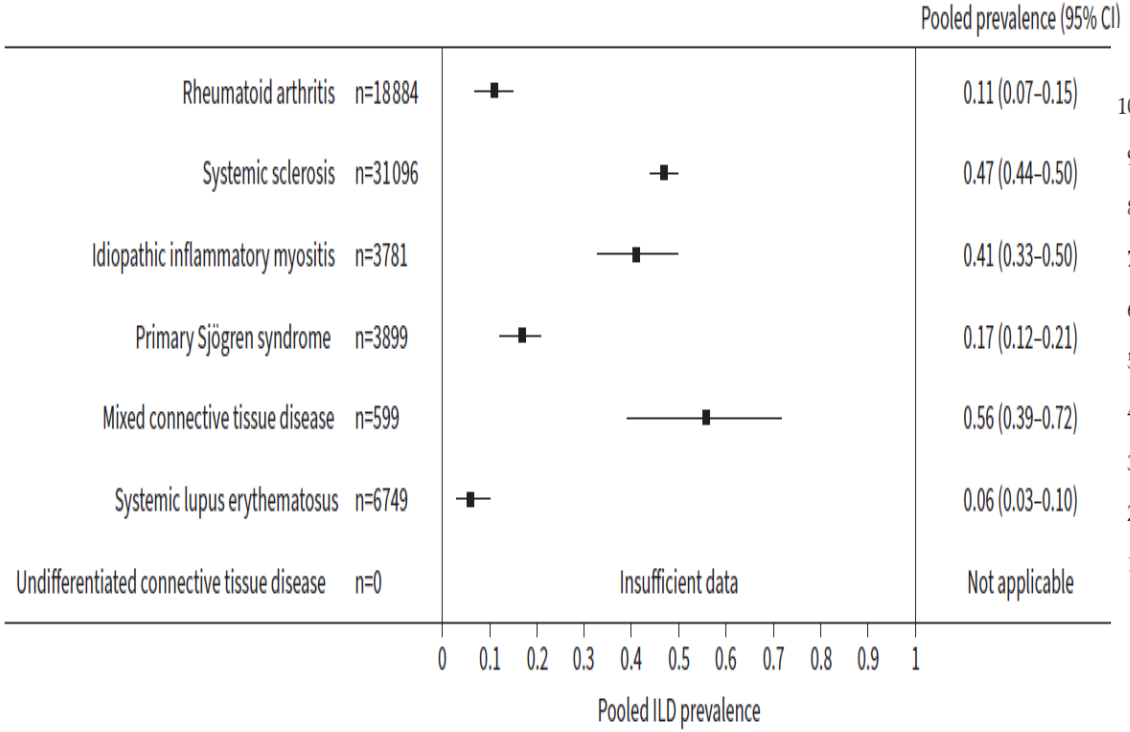
- ACR/CHEST(USA) guideline, 2024
- ERS/EULAR guideline, 2026
- 일본 가이드라인, 2026
- RCT, observational study
- 우리나라 보험 기준

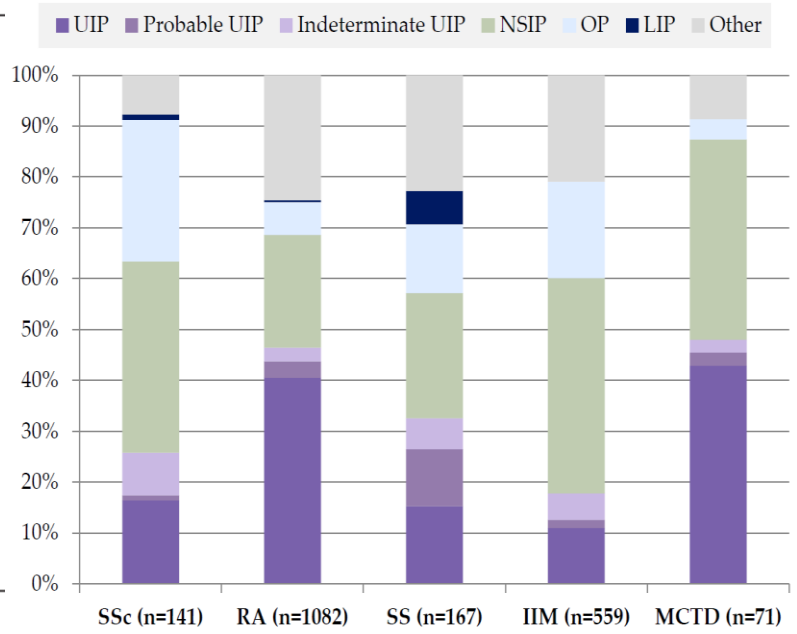
# Screening

# Screening

Prevalence: 2000~2022, 237 articles included

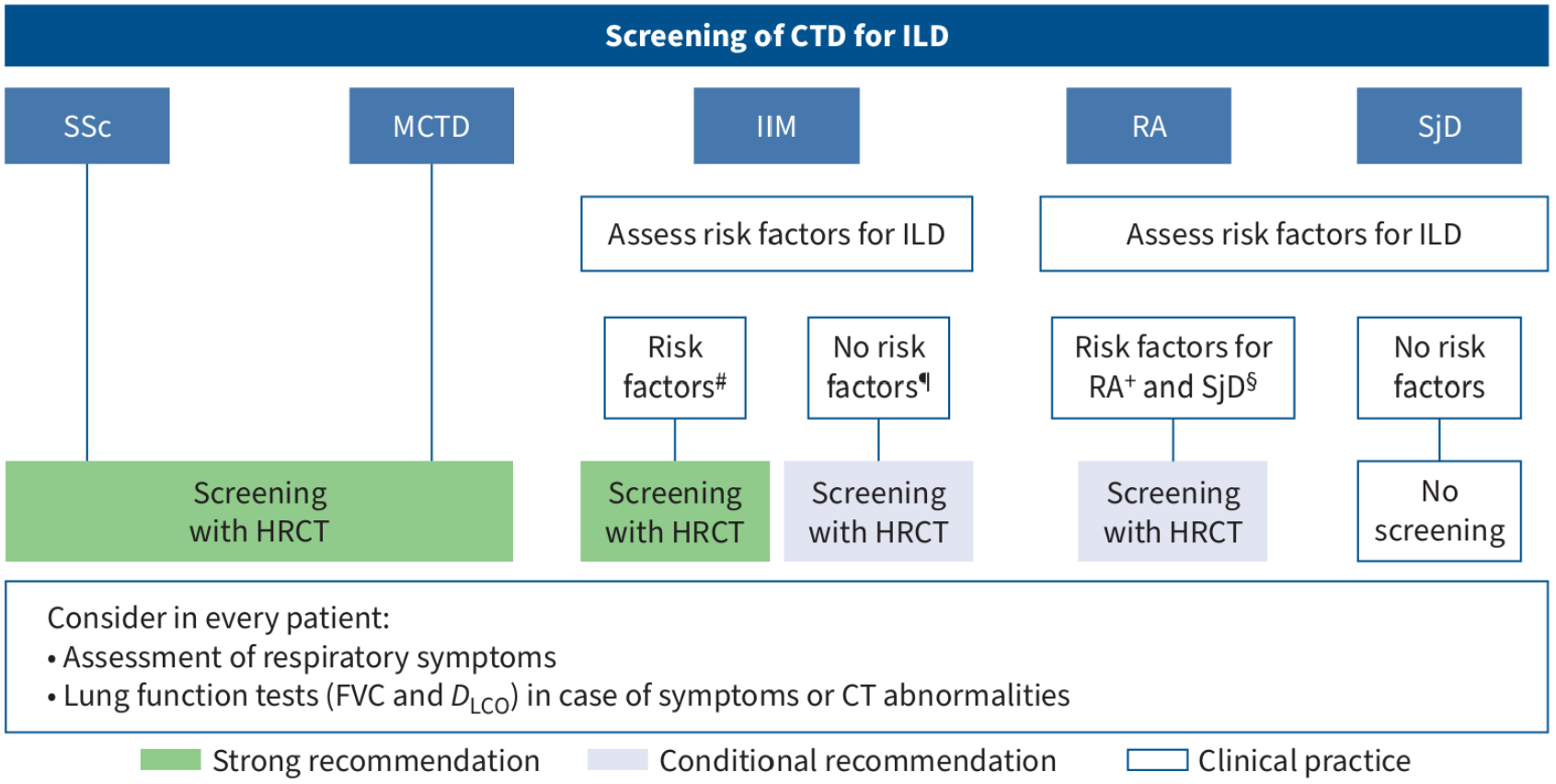
ILD Pattern : 2015~2024, 23 articles included




*Eur Respir Rev 2023; 32: 220210*
*J Clin Med 2025;14: 6164*

# Screening




*Eur Respir J 2026; 67: 2402533*

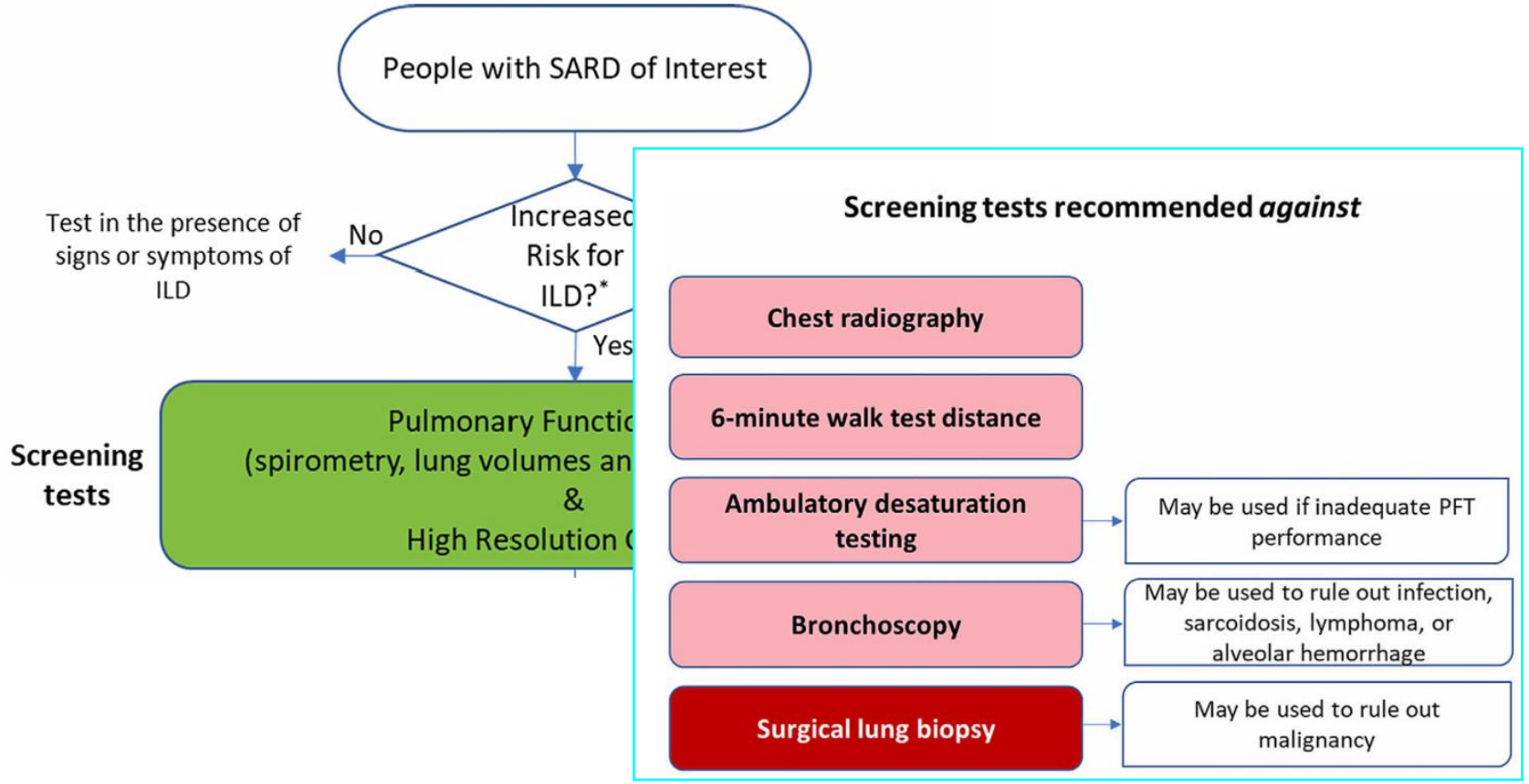
# Screening

**TABLE 3** Risk factors in patients with connective tissue disease and rheumatoid arthritis (RA) defining an at-risk patient population that should be screened for interstitial lung disease

| | SSc | RA | IIM | SjD |
|---|---|---|---|---|
| **Demographics** | • Longer disease duration | • Older age<br>• Male sex<br>• Smoking | • Older age | • Older age<br>• Male sex |
| **Circulating markers** | • Increased KL-6<br>• Presence of ATA-I | • Increased ESR<br>• Presence of anti-CCP, RF | • Increased CRP, ESR<br>• Presence of anti-Jo1, anti-MDA-5, anti-Ro52 | • Increased CRP<br>• Presence of anti-Ro52 |
| **Extrapulmonary involvement** | • Diffuse cutaneous SSc<br>• Higher mRSS | • Higher articular disease activity | • Anti-synthetase syndrome<br>• Clinical amyopathic dermatomyositis<br>• Skin involvement[#]<br>• Arthritis/arthralgia | • Presence of extrapulmonary involvement |

*Eur Respir J 2026; 67: 2402533*

# Screening




*Arthritis Rheumatol 2024; 76: 1201-1213*

# Screening

| Disease | Risk factors |
|---|---|
| Systemic sclerosis | • Anti–Scl-70 positivity, antinuclear antibody with nucleolar pattern[13]<br>• Diffuse cutaneous subtype, male sex, African American race[14,15]<br>• Early disease (first 5–7 y after onset)<br>• Elevated acute phase reactants[13,16] |
| Rheumatoid arthritis | • High-titer rheumatoid factor, high-titer anti-CCP[17–19]<br>• Cigarette smoking,[20,21] older age at rheumatoid arthritis onset,[22,23] high disease activity<br>• Male sex,[22] higher body mass index |
| Idiopathic inflammatory myopathies | • Anti-synthetase (Jo-1, PL7, PL12, EJ, OJ, KS, Ha, Zo), anti–MDA-5, anti-Ku, anti-Pm/Scl, anti-Ro52 antibody positivity<br>• Mechanic's hands, arthritis/arthralgia, ulcerating lesions[24] |
| Mixed connective tissue disease | • Dysphagia, Raynaud phenomenon<br>• Other systemic sclerosis clinical or laboratory features |
| Sjögren disease | • Anti-Ro52 antibody, antinuclear antibody[25,26]<br>• Raynaud phenomenon<br>• Older age<br>• Lymphopenia<br>• Severe dental caries |

*Arthritis Rheumatol 2024; 76: 1201-1213*

# Screening

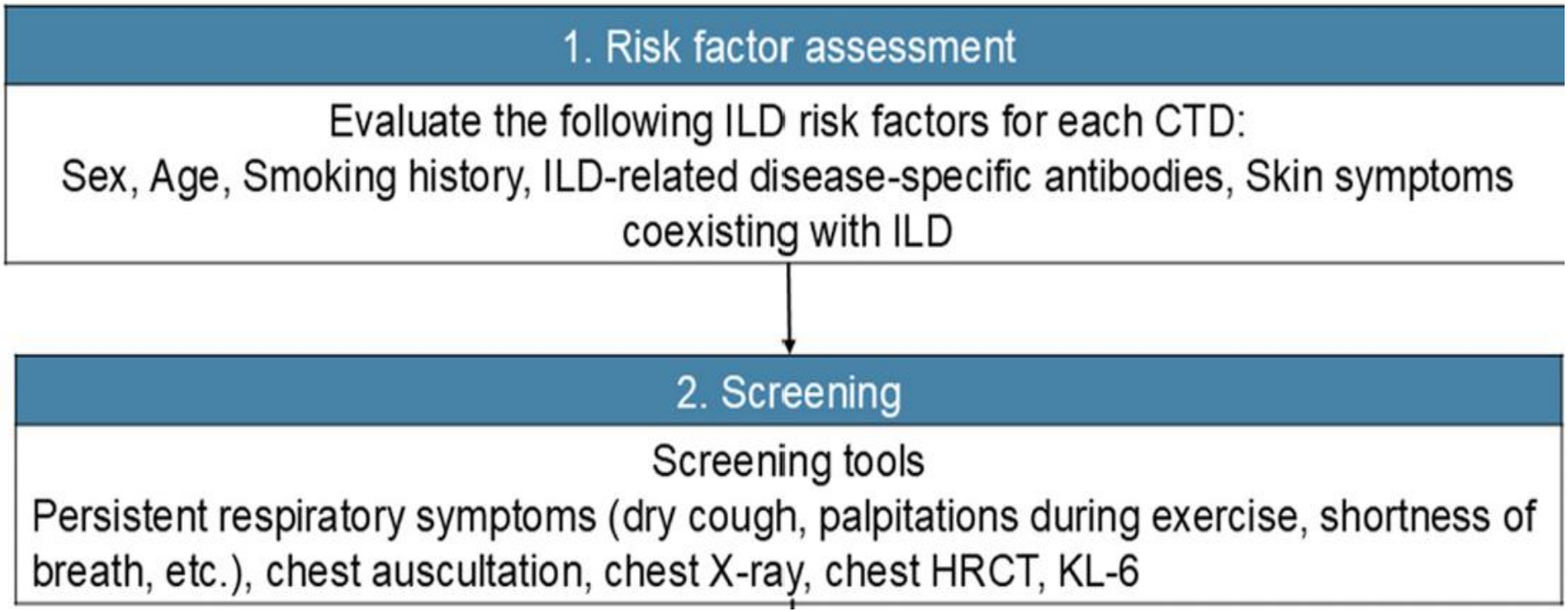
- Screening for ILD should not be limited to those with just these risk factors.

  The patient panel expressed a preference for identifying ILD early.

  If there is uncertainty regarding whom to screen, clinicians should proceed with screening for ILD.

*Arthritis Rheumatol 2024; 76: 1201-1213*

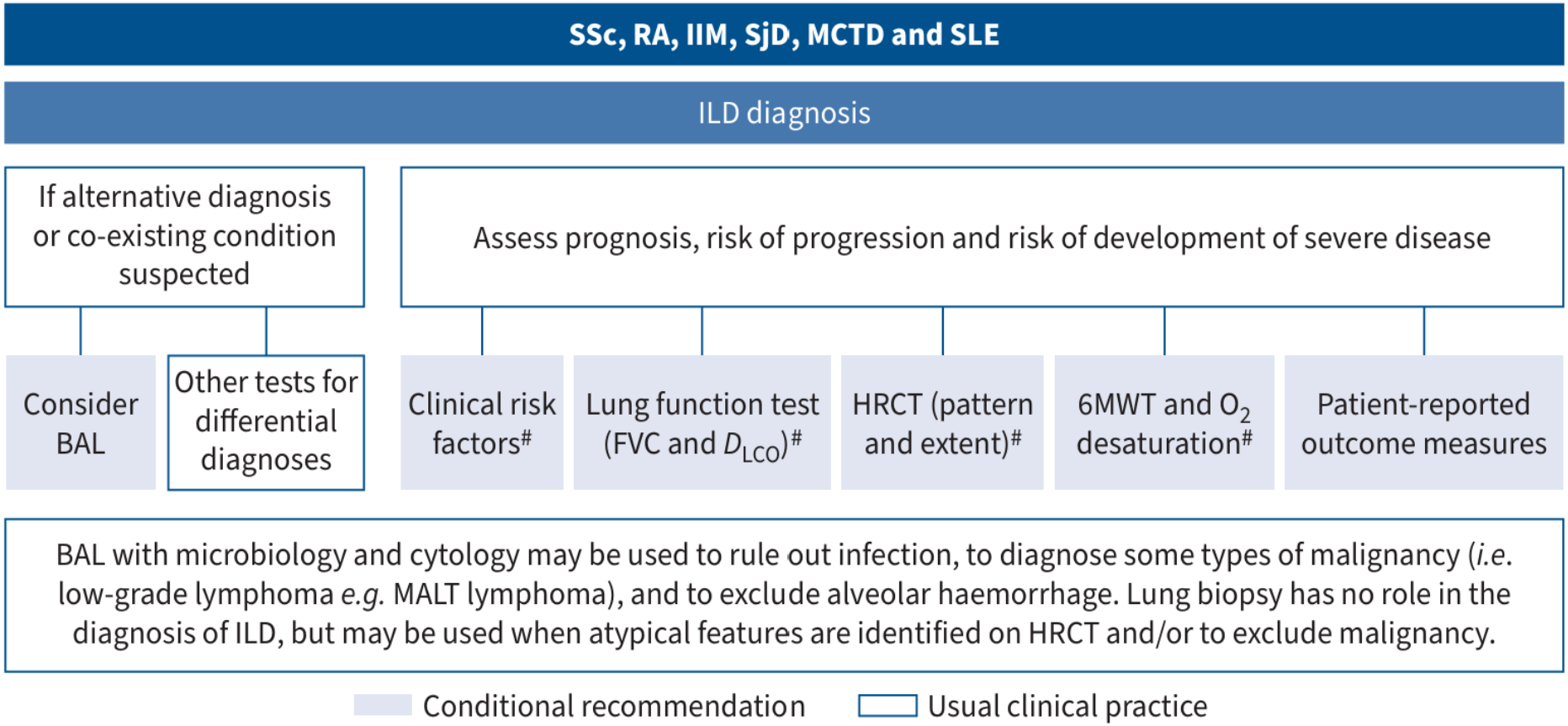
# Screening




*Respiratory Investigation 2026; 64: 101412*

# Diagnosis & Monitoring

# Diagnosis & Monitoring




*Eur Respir J 2026; 67: 2402533*

# Diagnosis & Monitoring

**TABLE 4** Risk factors for poor outcome, defined as disease progression and death, in patients with connective tissue disease (CTD)-associated interstitial lung disease (ILD) and rheumatoid arthritis (RA)-associated ILD

| | SSc[#] | RA[#] | IIM[#,¶] |
|---|---|---|---|
| **Demographics** | • Older age<br>• Male sex<br>• African American ethnicity | • Older age at RA onset<br>• Male sex | |
| **Circulating markers** | • Elevated ESR, CRP<br>• ATA-I | • Anti-CCP, RF | • Elevated ferritin<br>• Anti-MDA-5, anti-synthetase |
| **Pulmonary function/markers** | • Baseline PFTs (FVC, $D_{LCO}$) | • Baseline PFTs (low FVC and/or $D_{LCO}$) | |
| **Imaging/histology** | • Higher extent of ILD on HRCT | • UIP and probable UIP HRCT/histological patterns<br>• Higher extent of ILD on HRCT | • Higher extent of ILD on HRCT and ILD pattern on HRCT |
| **Extrapulmonary involvement** | • Recent onset of SSc with rapid skin progression, more extensive skin fibrosis (mRSS) | • Higher articular disease activity | |

*Eur Respir J 2026; 67: 2402533*

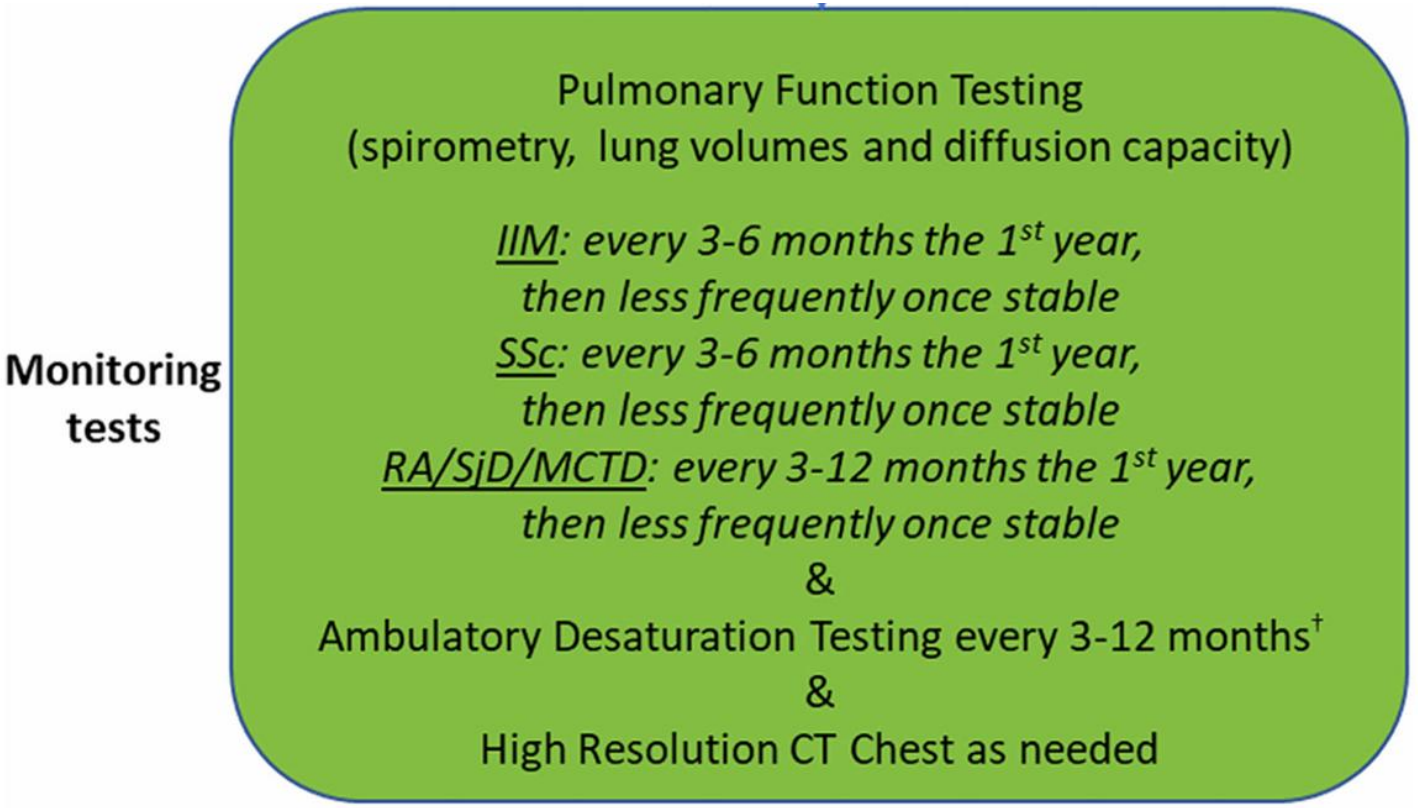
# Diagnosis & Monitoring

- PFT(FVC, $DL_{CO}$)
  - SSc : q 3~6 months during 3-5yr → 6~12 months
  - RA : q 3~6 months during 1-2yr → 6~12 months ($FEV_1$ 포함)
  - IIM : q 3~6 months during 1 yr → 6~12 months (progression 의심시)
  - Sjögren's dz : q 3~6 months during 1yr → 6~12 months (progression 의심시)
  - SLE, MCTD : No recommendation

- CT
  - SSc, RA : repeat HRCT after 1-2 yr (progression 의심시)
  - IIM : repeat HRCT after 3~6 months at risk of developing RP-ILD → annually repeat over 2 yrs
  - other CTD: repeat HRCT after 1-2 yr

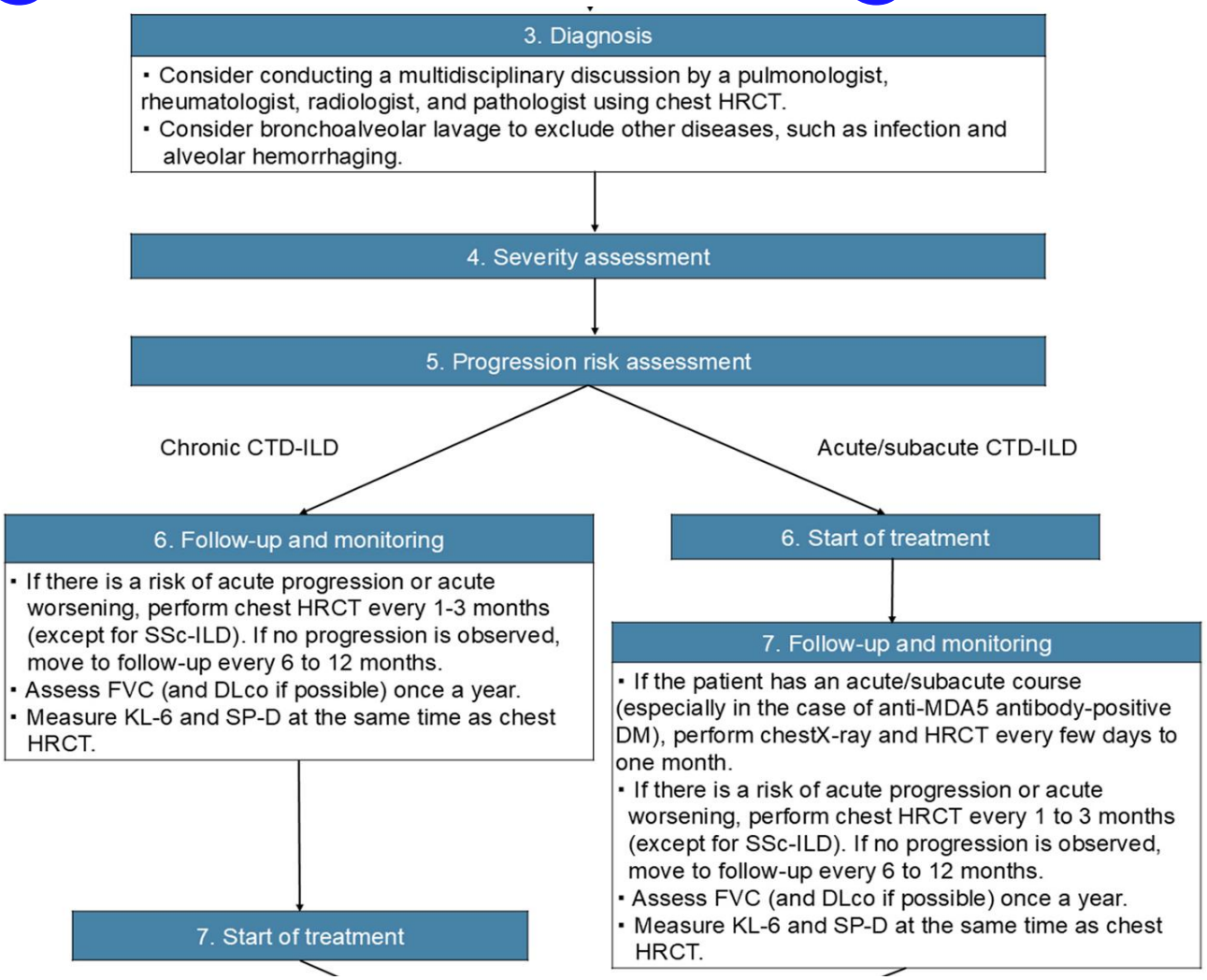
*Eur Respir J 2026; 67: 2402533*

# Diagnosis & Monitoring




*Arthritis Rheumatol 2024; 76: 1201-1213*

# Diagnosis & Monitoring




*Respiratory Investigation 2026; 64: 101412*

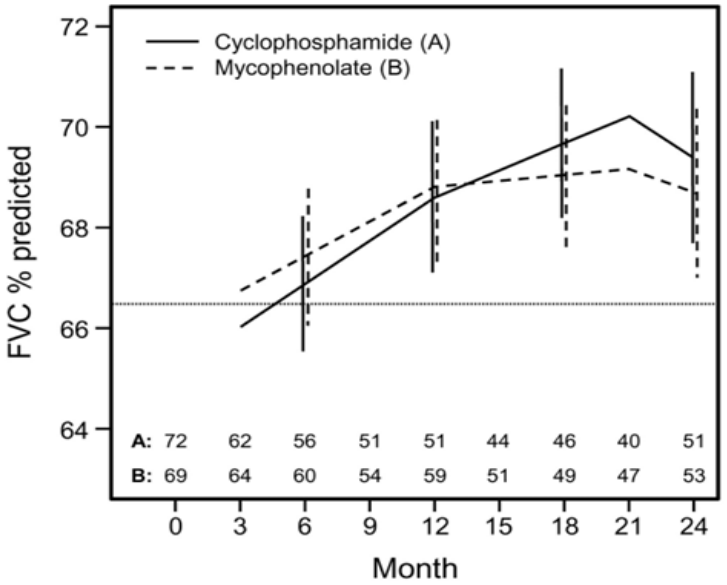
# Treatment

# SLS II (SSc, MMF vs cyclophosphamide)

- 2009.11~2013.1, double blind, RCT, USA
- SSc-ILD: 80% >FVC > 45%, non-Raynaud's Sx< 7yr
- Primary outcome: FVC % at 2yr

Randomization (n=142)

- cyclophosphamide (n=73) for 1yr → placebo 1yr
- MMF (n=69) for 2 yrs




*Lancet Respir Med 2016; 4: 708-19*

# faSScinate (SSc, tocilizumab)

- 2012.3~2013.6, double blind,RCT, EU+USA
- Progressive SSc: non-Raynaud's Sx< 5yr, new onset,
  skin aggravation, increased ESR/CPR/Plt
- Primary outcome: mean change in mRSS (24wk)

Randomization (n=87)
- tocilizumab (n=43), sc, weekly
- placebo (n=44)

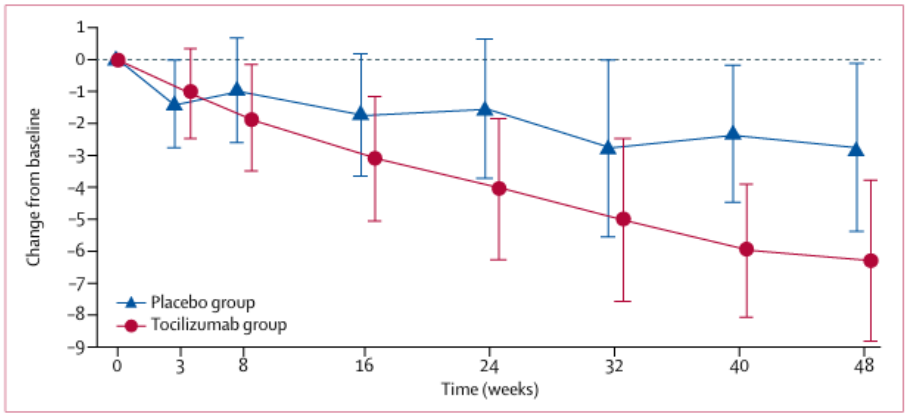



*Figure 2:* Change (95% CI) from baseline in modified Rodnan skin score

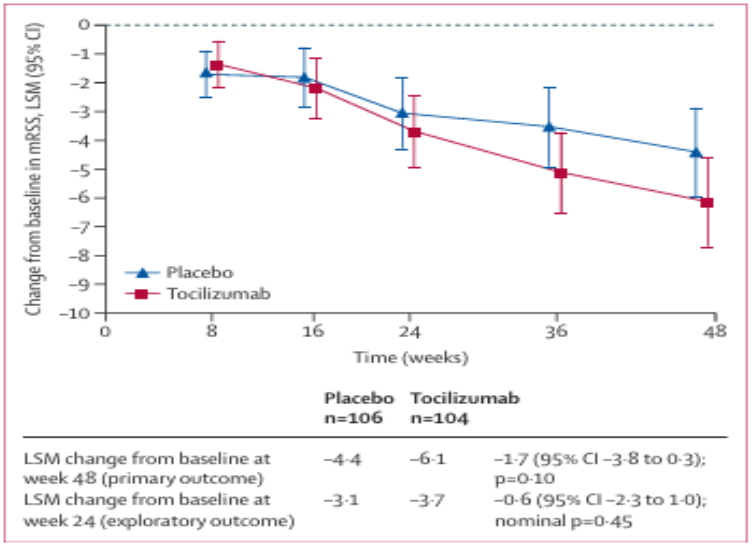
Δ FVC at 24 wk
: -34ml (tocilizumab)
-171ml(placebo)
(p=0.0368)

*Lancet 2016; 387: 2630-40*

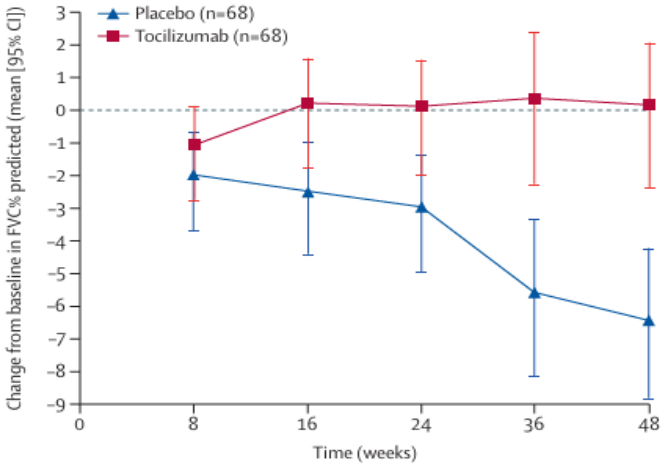
# focuSSced (SSc, tocilizumab)

- 2015.11~2017.2, double blind, RCT, EU+America+Japan
- Early dcSSc: non-Raynaud's Sx< 5yr, increased ESR/CPR/plt, FVC ≥55%, $DL_{CO}$ ≥45%
- Primary outcome: mean change in mRSS (48wk)

Randomization (n=210)
- tocilizumab (n=104)
- placebo (n=106)




| | Placebo n=106 | Tocilizumab n=104 | |
|---|---|---|---|
| LSM change from baseline at week 48 (primary outcome) | −4·4 | −6·1 | −1·7 (95% CI −3·8 to 0·3); p=0·10 |
| LSM change from baseline at week 24 (exploratory outcome) | −3·1 | −3·7 | −0·6 (95% CI −2·3 to 1·0); nominal p=0·45 |

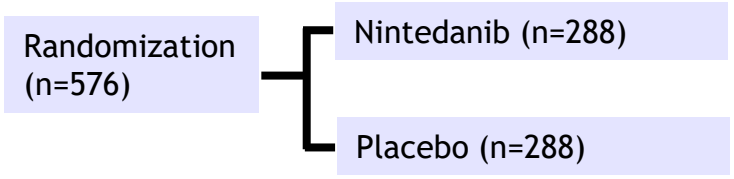


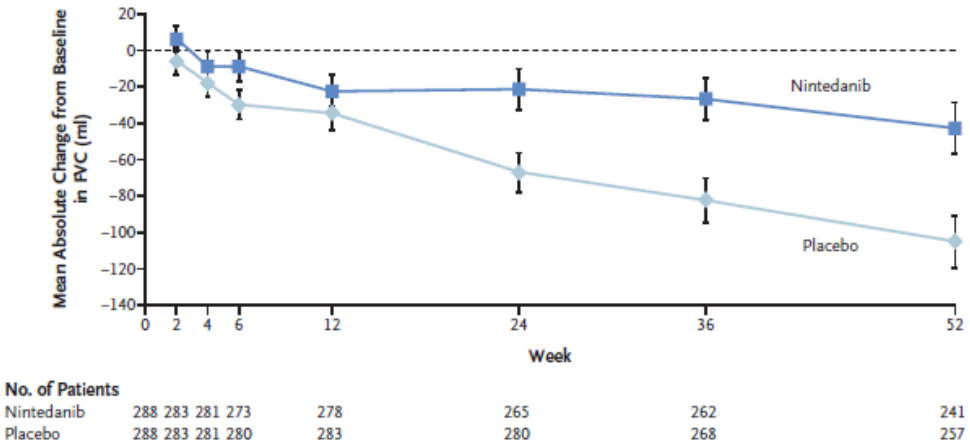

*Lancet Respir Med 2020; 8: 963-74*

# SENSIS (SSc, Nintedanib)

- 2015.11~2017.10, double blind, RCT, EU+ America + Asia
- SSc-ILD: non-Raynaud's Sx< 7yr, fibrosis ≥ 10%(CT)

  FVC ≥40%, 89% ≥$DL_{CO}$ ≥30%
- Primary outcome: ΔFVC % at 52 wk




MMF(+)

-40.2ml (nintedanib)

-66.5ml (placebo)

MMF(-)

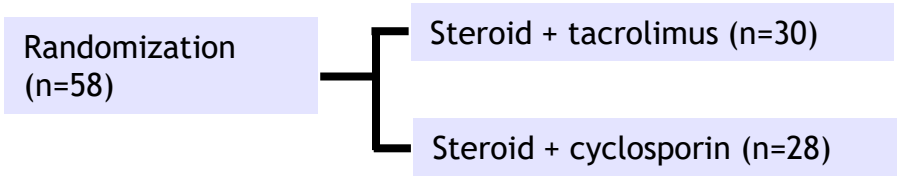
-63.9ml (nintedanib)

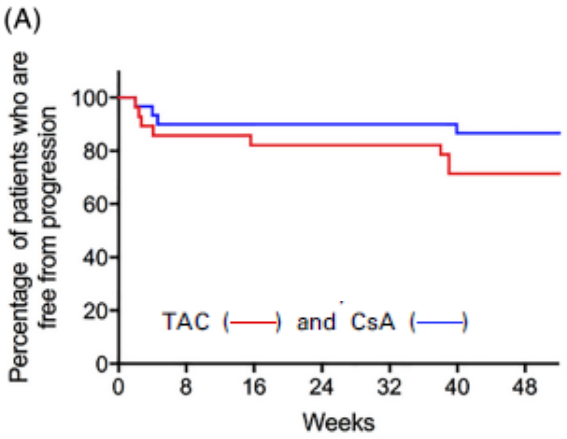
-119.3ml (placebo)

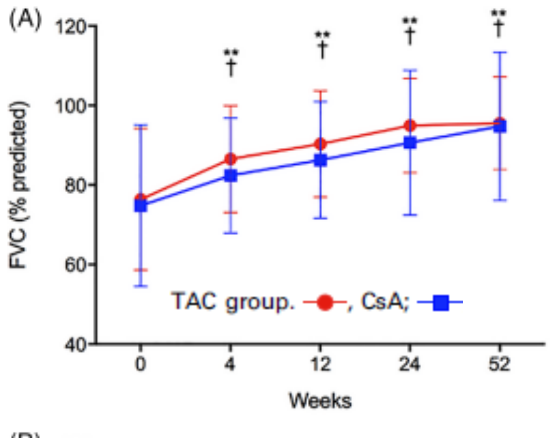
*N Engl J Med 2019; 380: 2518-28*

# DM, PM (tacrolimus vs cyclosporin)

- 2014.11~2018.3, open label, RCT, Japan
- DM/PM/CADM-ILD
- Primary outcome:  Progression Free Survival rate at 52 wk




PFS
- Tacro (87%)
- CsA ( 71%)

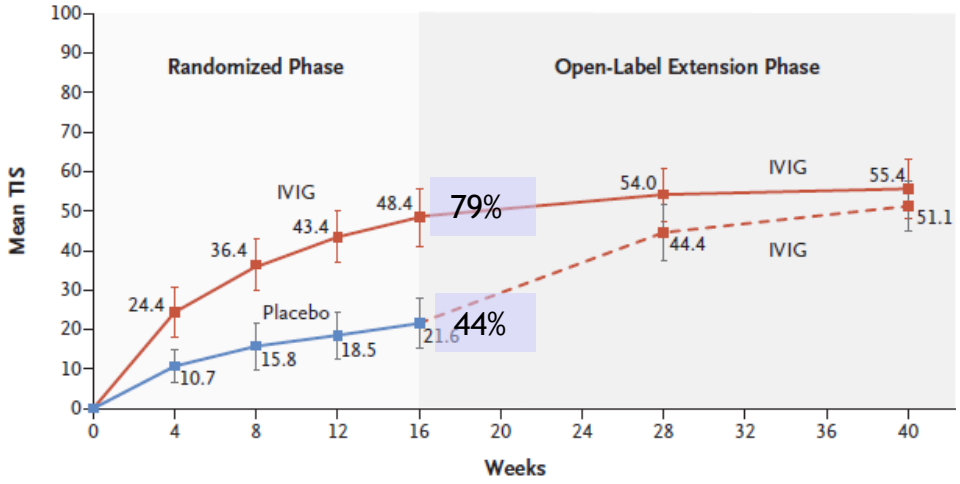
*Respirology 2021; 26: 370-377*

# ProDERM (DM, IVIG)

- 2017.2~2019.11, double blind, RCT, EU + North America
- Dermatomyositis (proximal m weakness+ rash)
- Primary outcome: Total Improvement Score(≥20) at 16 wk

Randomization (n=96)

- IVIG (n=47, 2g/kg q 4 wk, 4 times)
- Placebo (n=48)



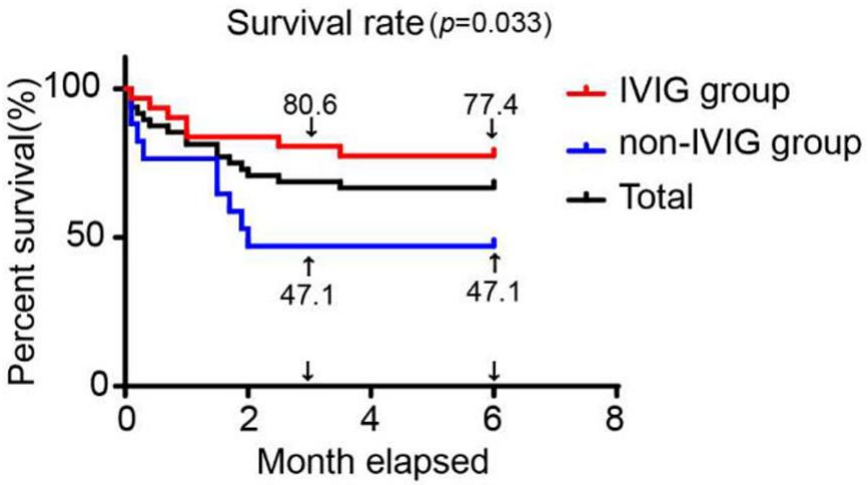

*N Engl J Med 2022; 387: 1264-78*

# MDA 5(+) RP-ILD (IVIG)

- 2018.9~2020.6, Retrospective, China
- Anti MDA 5(+) RP-ILD (DM/CADM)
- Primary outcome: 3,6-month mortality

IVIG (n=31) +high dose steroid + immunosuppressant(CNI, CYC, Rituximab..)

Non-IVIG (n=17) + high dose steroid + immunosuppressant(CNI, CYC, Rituximab..)



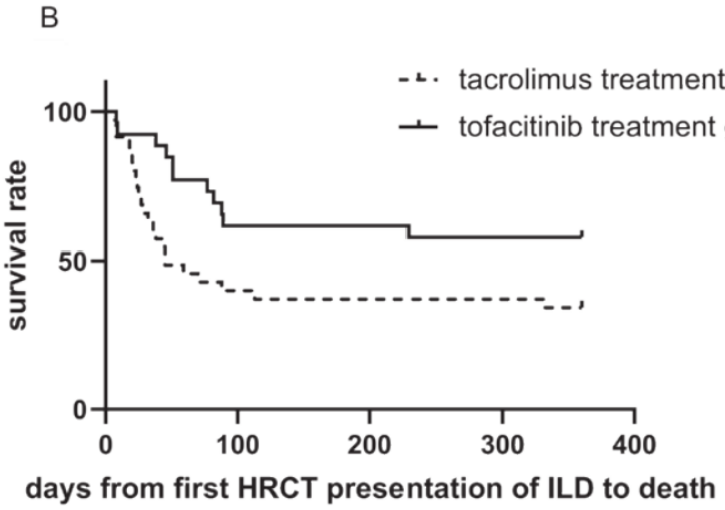

*Rheumatology 2022; 61: 3704-3710*

# MDA 5(+) ILD (JAKi vs tacrolimus)

- 2017.10~2020.12, Retrospective, China
- MDA 5(+) ILD
- Primary outcome: 6-month/ 1-yr mortality

JAKi (tofacitinib) (n=26, RP-ILD (n=13)) + steroid

Tacrolimus (n=35, RP-ILD (n=22)) + steroid




RP-ILD

- 6-month mortality
  - 76.9 % (JAKi)
  - 95.5 % (Tacro)
- 1-yr mortality
  - 84.6 % (JAKi)
  - 100 % (Tacro)

*J Rheumatology 2022; 49: 1356-1364*

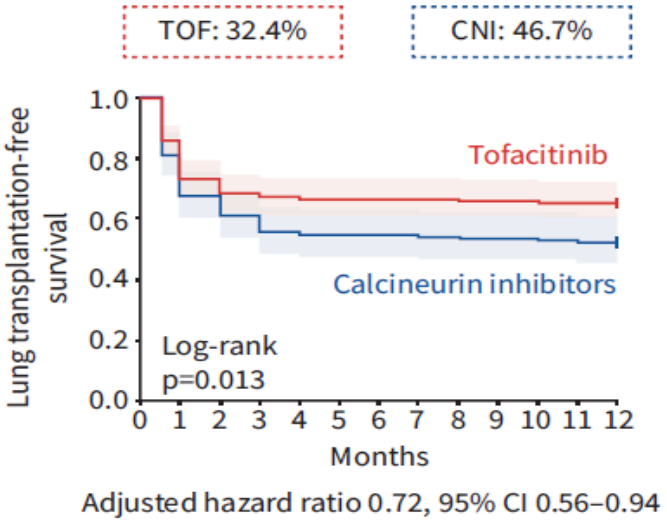
# MDA 5(+) ILD (JAKi vs CNI)

- 2014.4~2023.1, Retrospective cohort, China
- MDA 5(+) ILD (within 3 months)
- Primary outcome: lung transplantation-free survival (1yr)

JAKi (tofacitinib) (n=290, RP-ILD (52%)

CNI (tacrolimus or cyclosporine A) (n=225, RP-ILD (57%))

**Death or lung transplantation within 1 year**



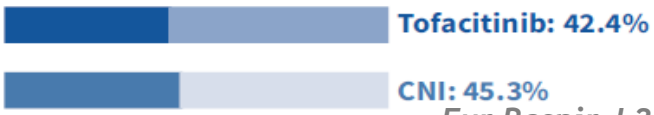

Adjusted hazard ratio 0.72, 95% CI 0.56–0.94

**Subgroup analysis**

Who might benefit more from tofacitinib:


**Severe adverse event within 1 year**

Overall infection rate:




*Eur Respir J 2025; 65: 2401488*

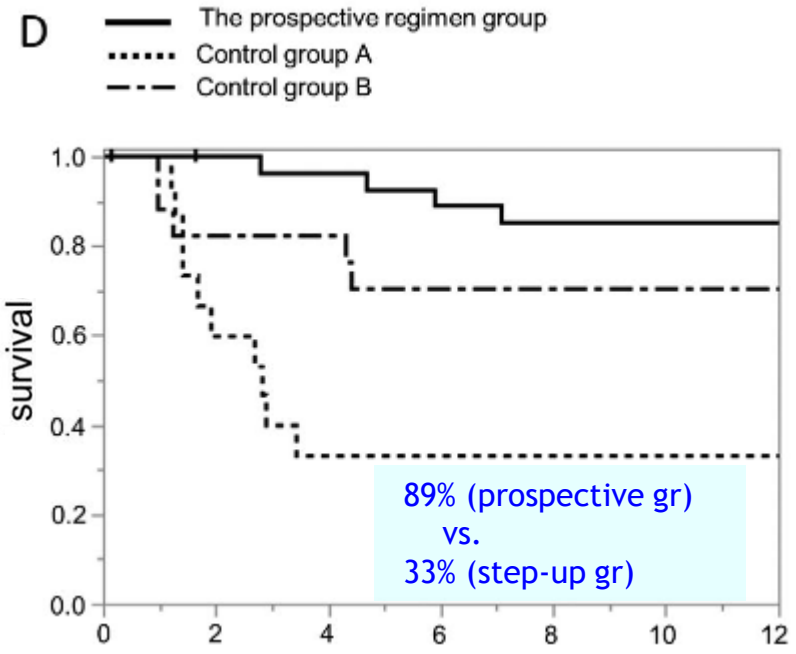
# MDA 5(+) DM/CADM (combination)

- 2014.7~2017.8, Prospective single arm study (vs historical gr), Japan
- Anti MDA 5(+) DM/CADM-ILD
- Primary outcome:  6-month survival rate

A prospective regimen gr (n=29)
: high dose steroid(1mg/kg/d, 4wk)
+ IV cyclophosphamide(500-1000mg/$m^2$) q 2wk
+ **tacrolimus**(10-12ng/ml(12 h trough))
± **plasmapheresis**

Historical control gr A (n=15) (2001.8~2008.12)
( Step-up treatment)
: high dose steroid
immunosuppressants were added stepwise

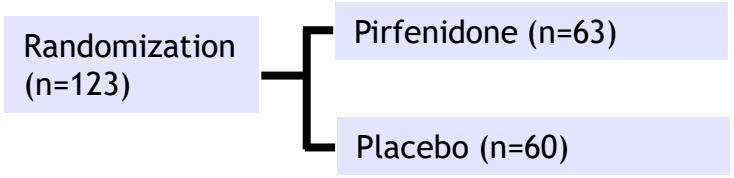
Historical control gr B (n=17) (2008.9~2013.2)
: high dose steroid(1mg/kg/d, 4wk)
+ IV cyclophosphamide
+ **cyclosporin A**
**without plasmapheresis**

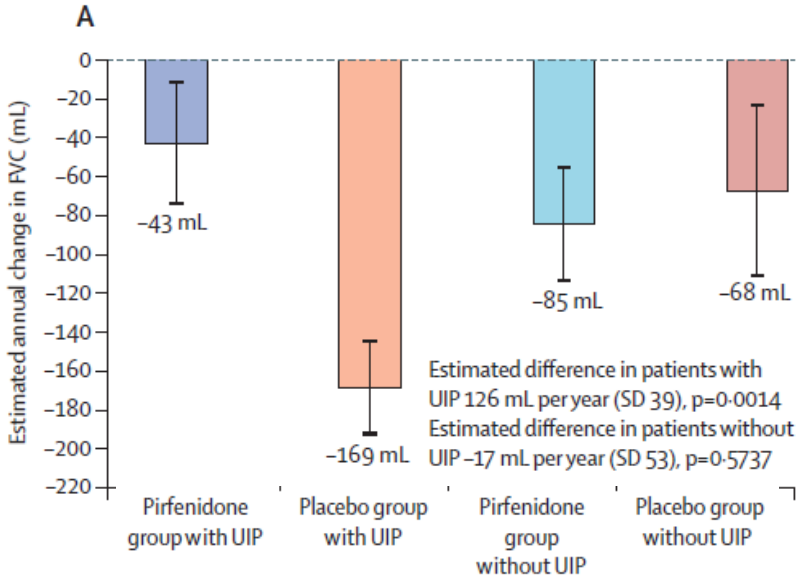


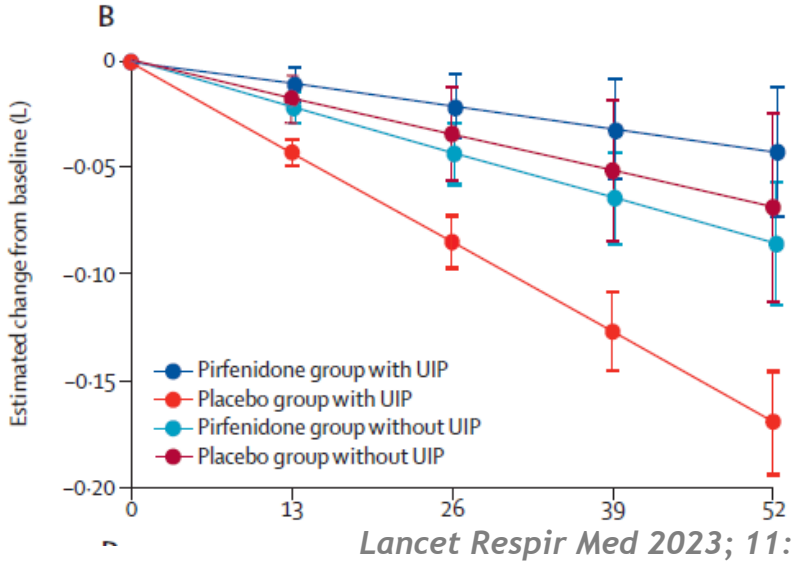

*Arthritis & Rheumatology 2020; 72: 488-498*

# TRAIL1 (RA, Pirfenidone)

- 2017.5~2020.3, double blind, RCT, UK+USA+Canada+Australia
- RA-ILD: fibrosis ≥ 10%(CT), FVC ≥40%, $DL_{CO}$ ≥30%
- Primary outcome: decline in FVC ≥ 10% or death during 52 wk



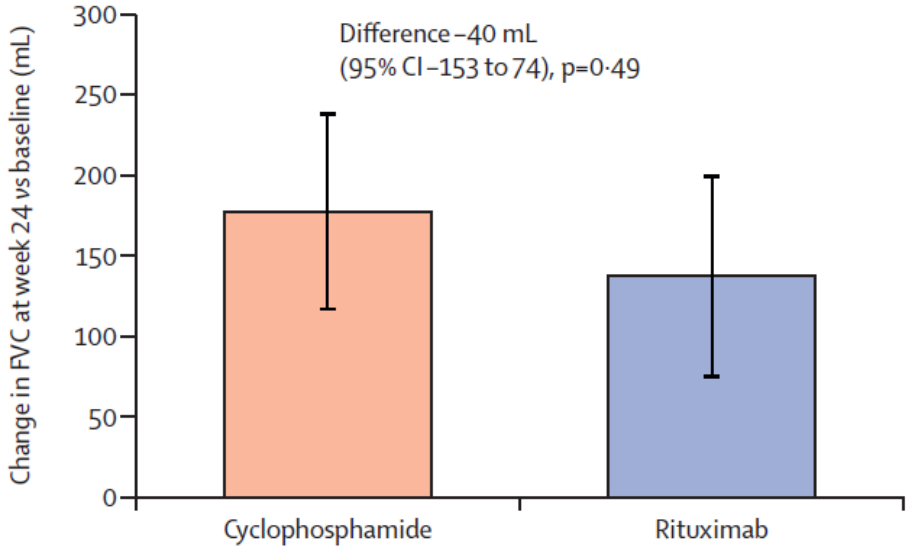

*Lancet Respir Med 2023; 11: 87-96*

# RECITAL(CTD, rituximab vs cyclophos)

- 2014.12~2020.3, double blind, RCT, UK
- Severe or progressive CTD-ILD (IIM(45%), SSc(40%), MCTD(15%))
- Primary outcome: ΔFVC % at 24 wk

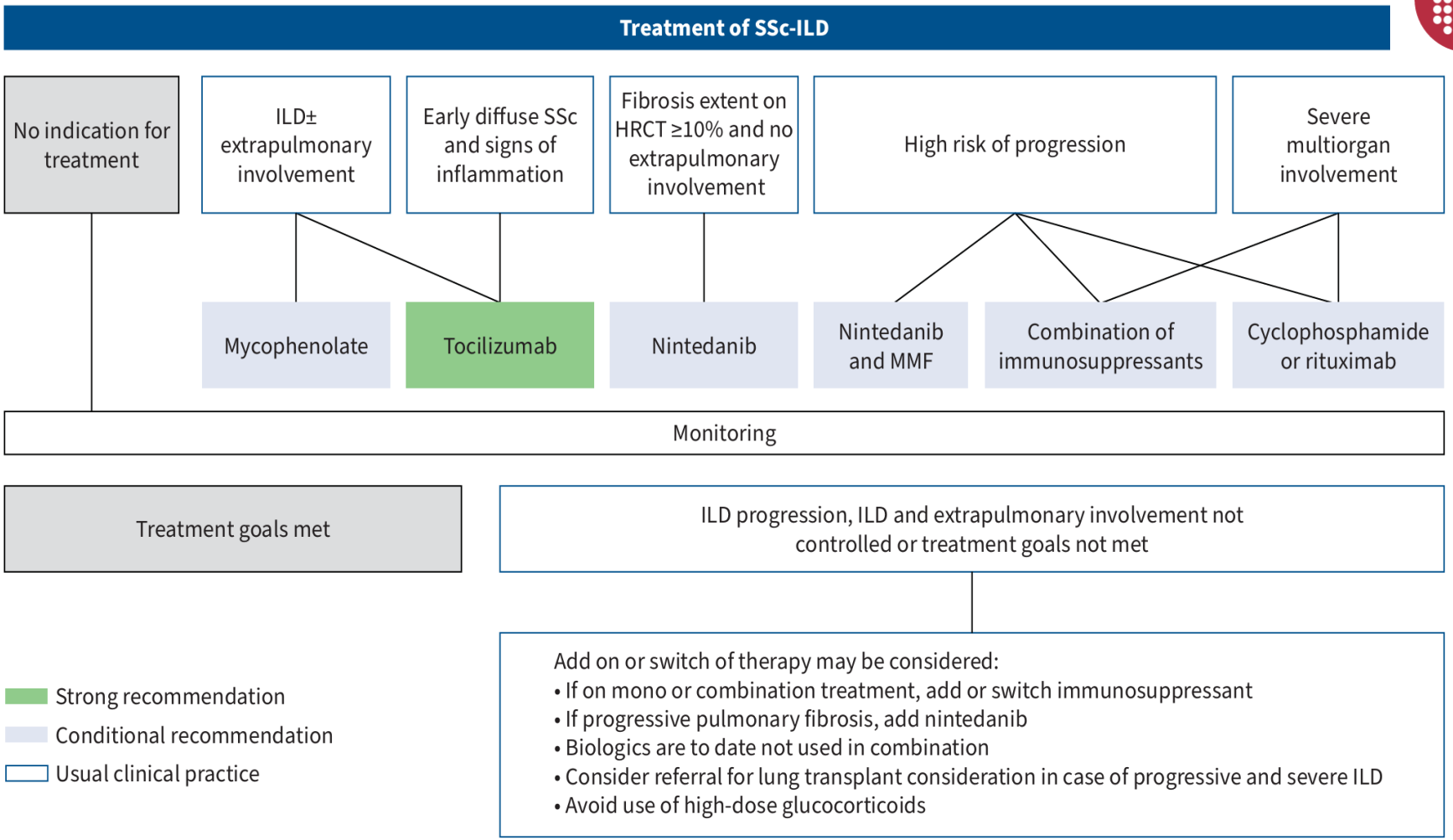
Randomization (n=101)

- Rituximab (n=51, day #0, 15)
- IV cyclophosphamide (n=50, q 4wk for 6 months)



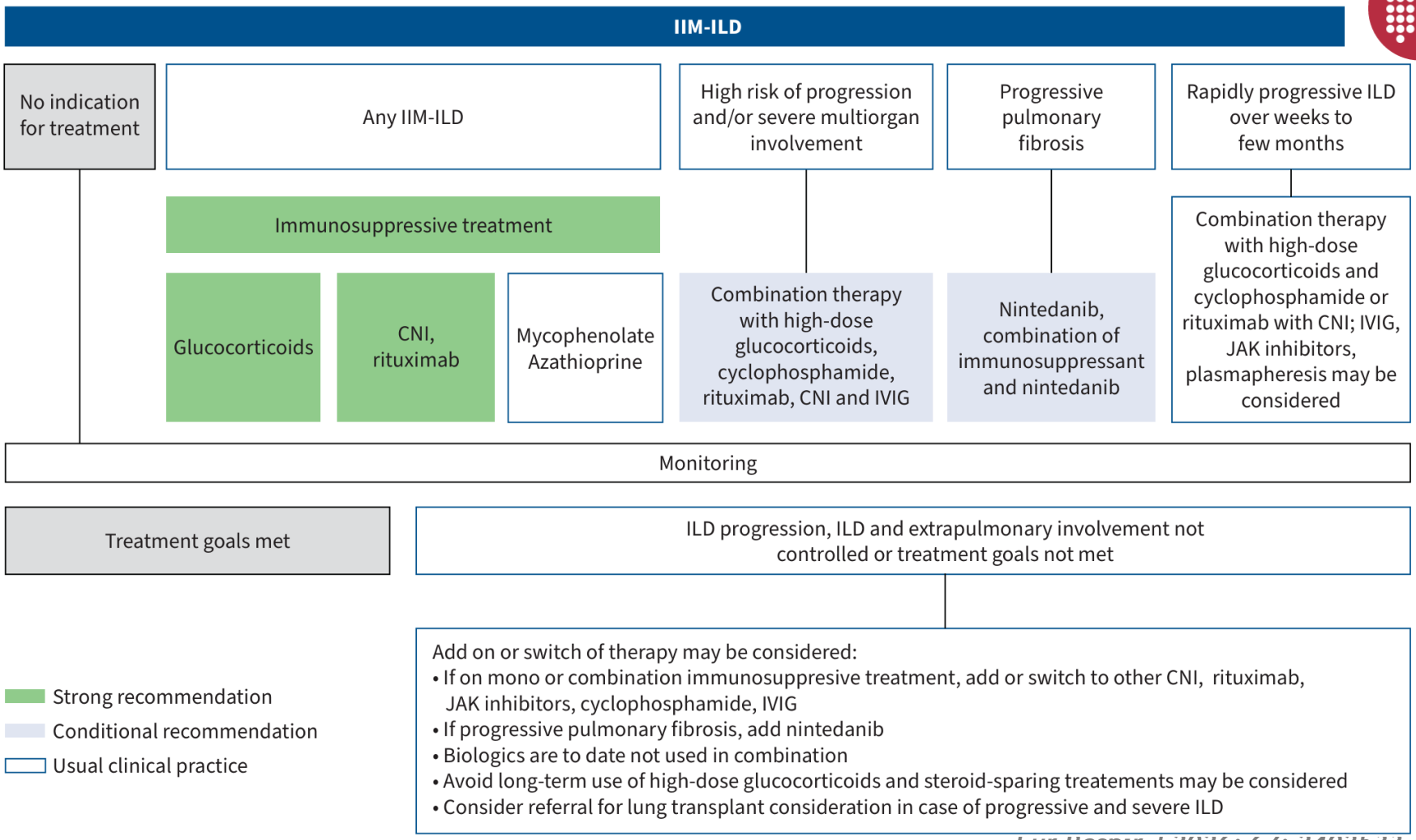

*Lancet Respir Med 2023; 11: 45-54*

# Treatment



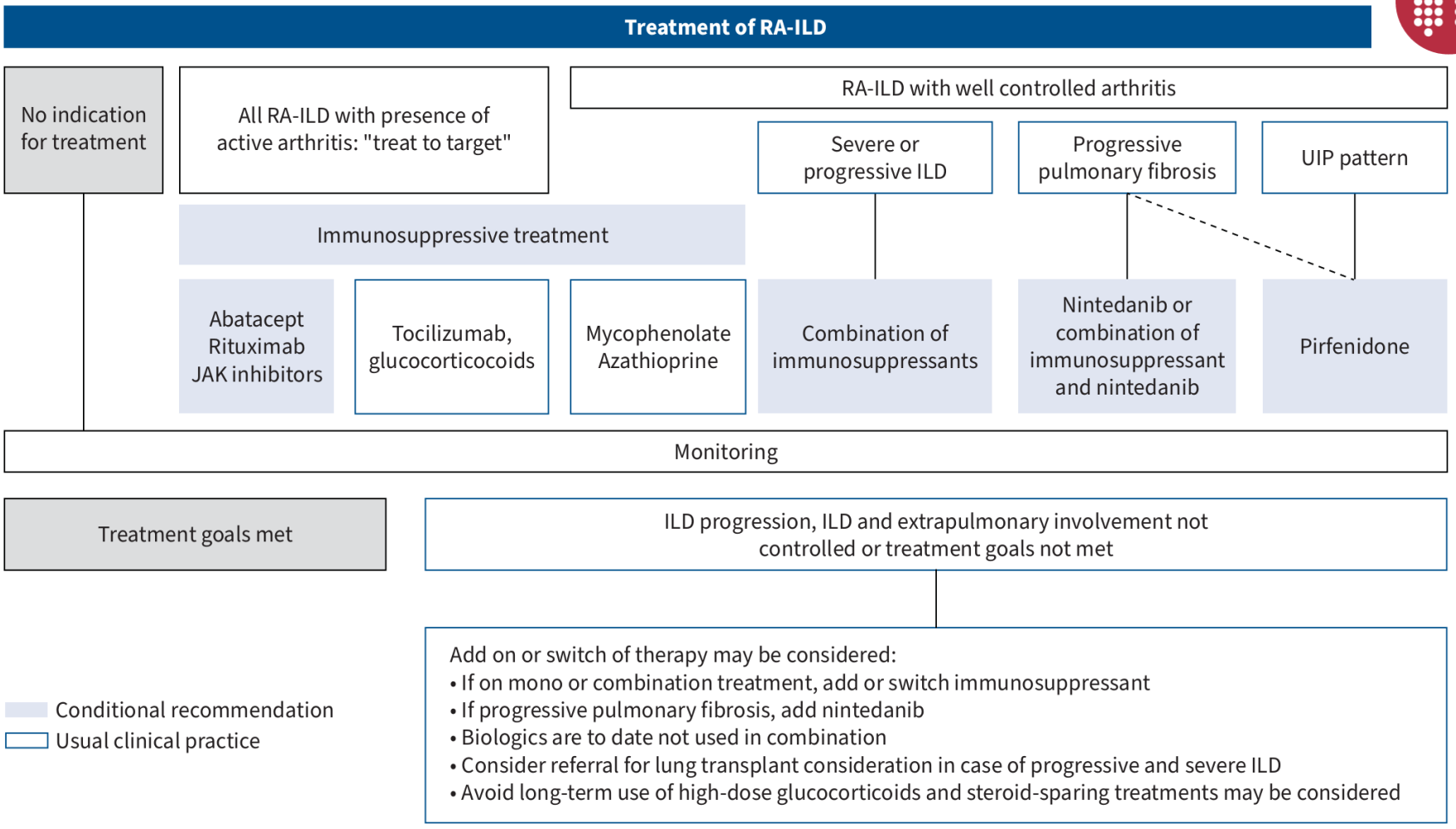

*Eur Respir J 2026; 67: 2402533*

# Treatment



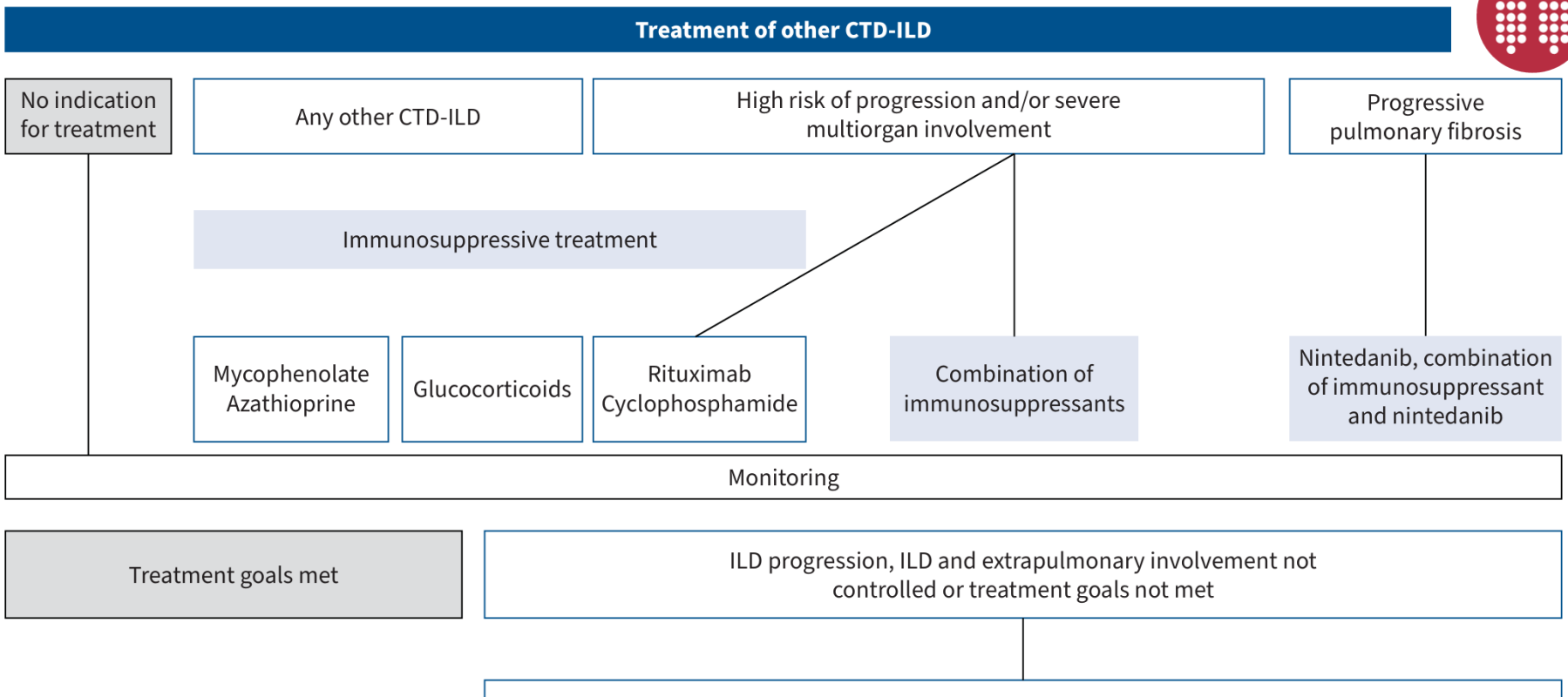

*Eur Respir J 2026; 67: 2402533*

# Treatment



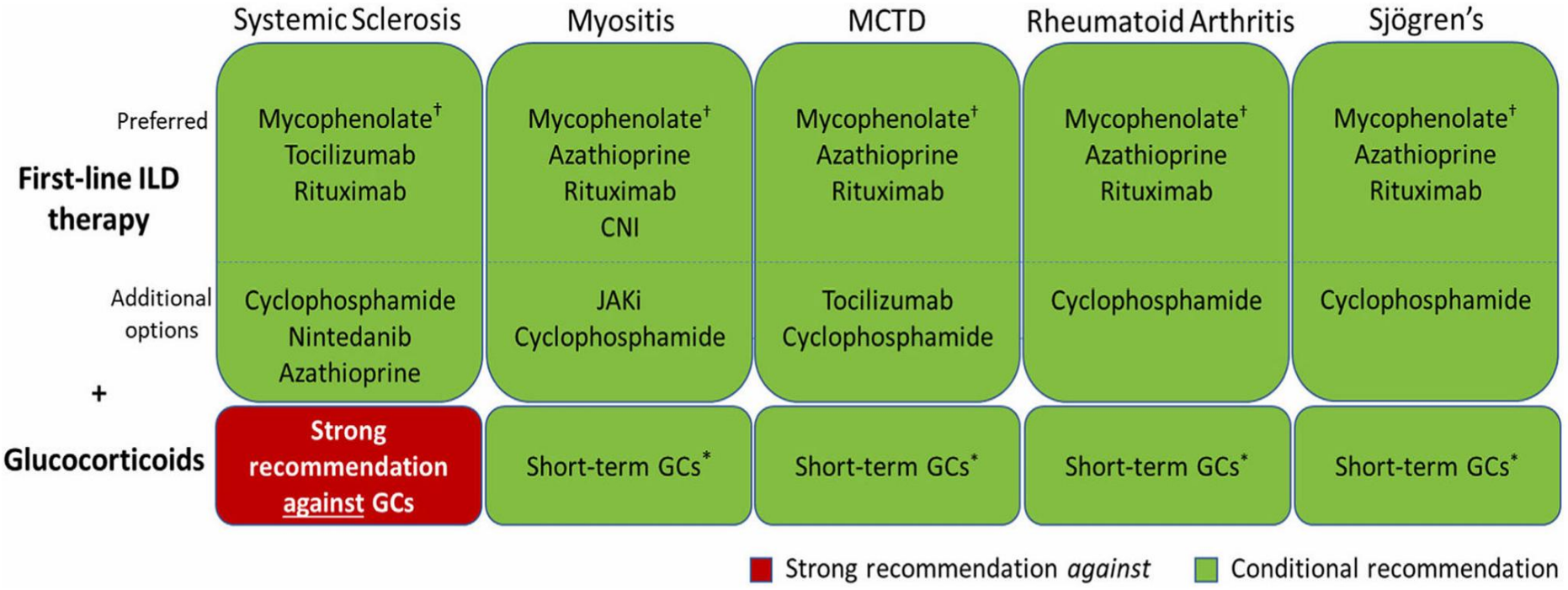

*Eur Respir J 2026; 67: 2402533*

# Treatment



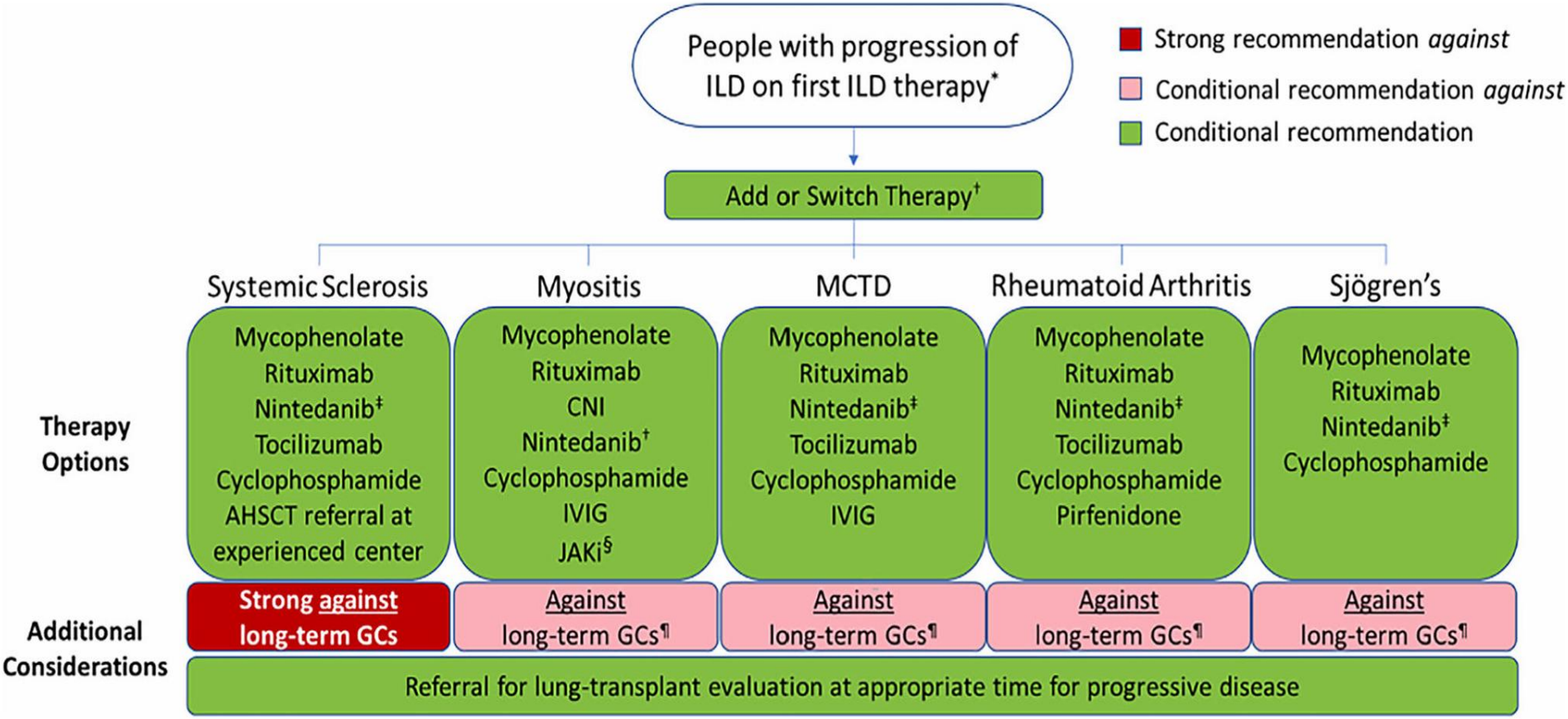

*Eur Respir J 2026; 67: 2402533*

# Treatment



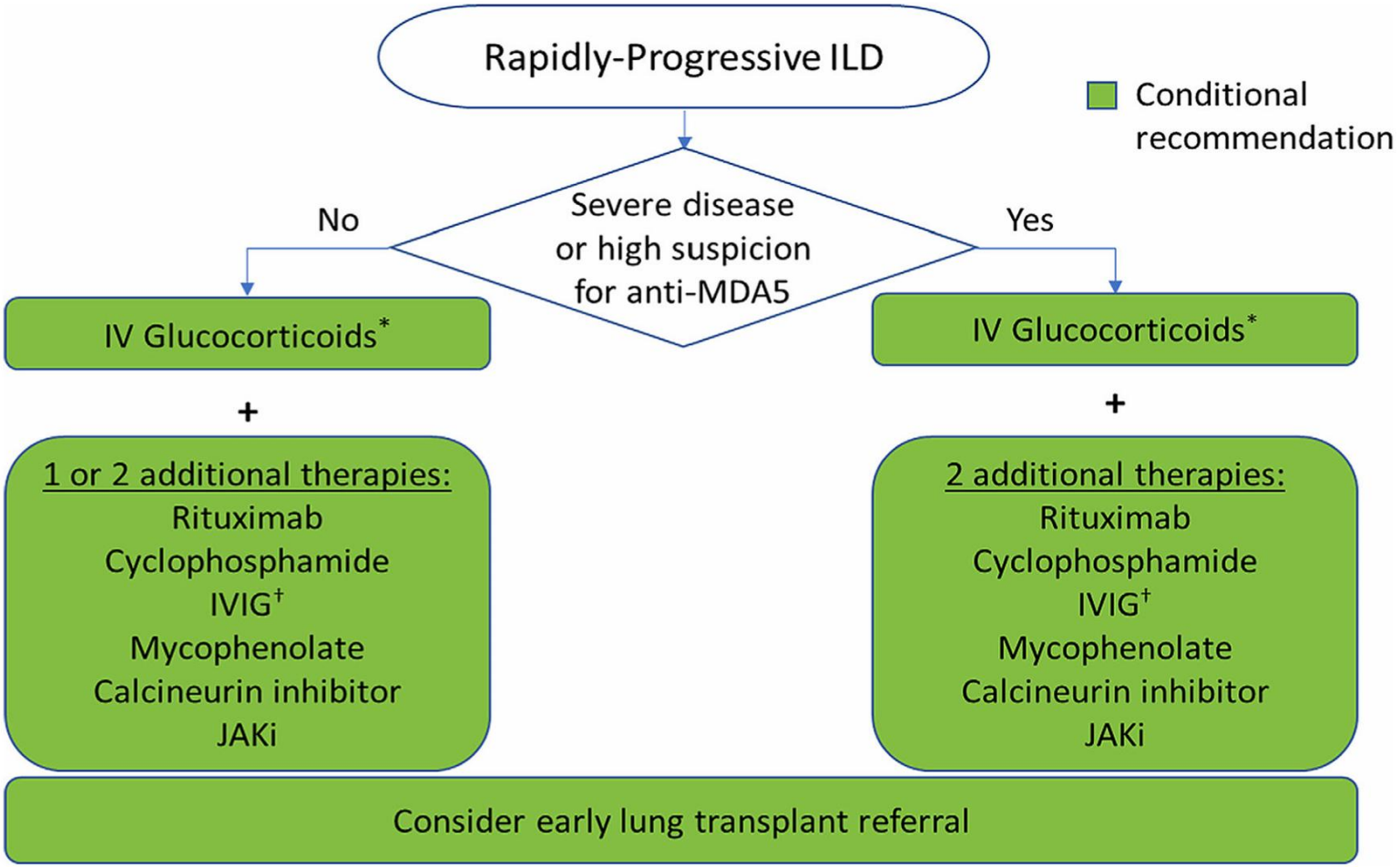

*Arthritis Rheumatol 2024; 76: 1201-1213*

# Treatment



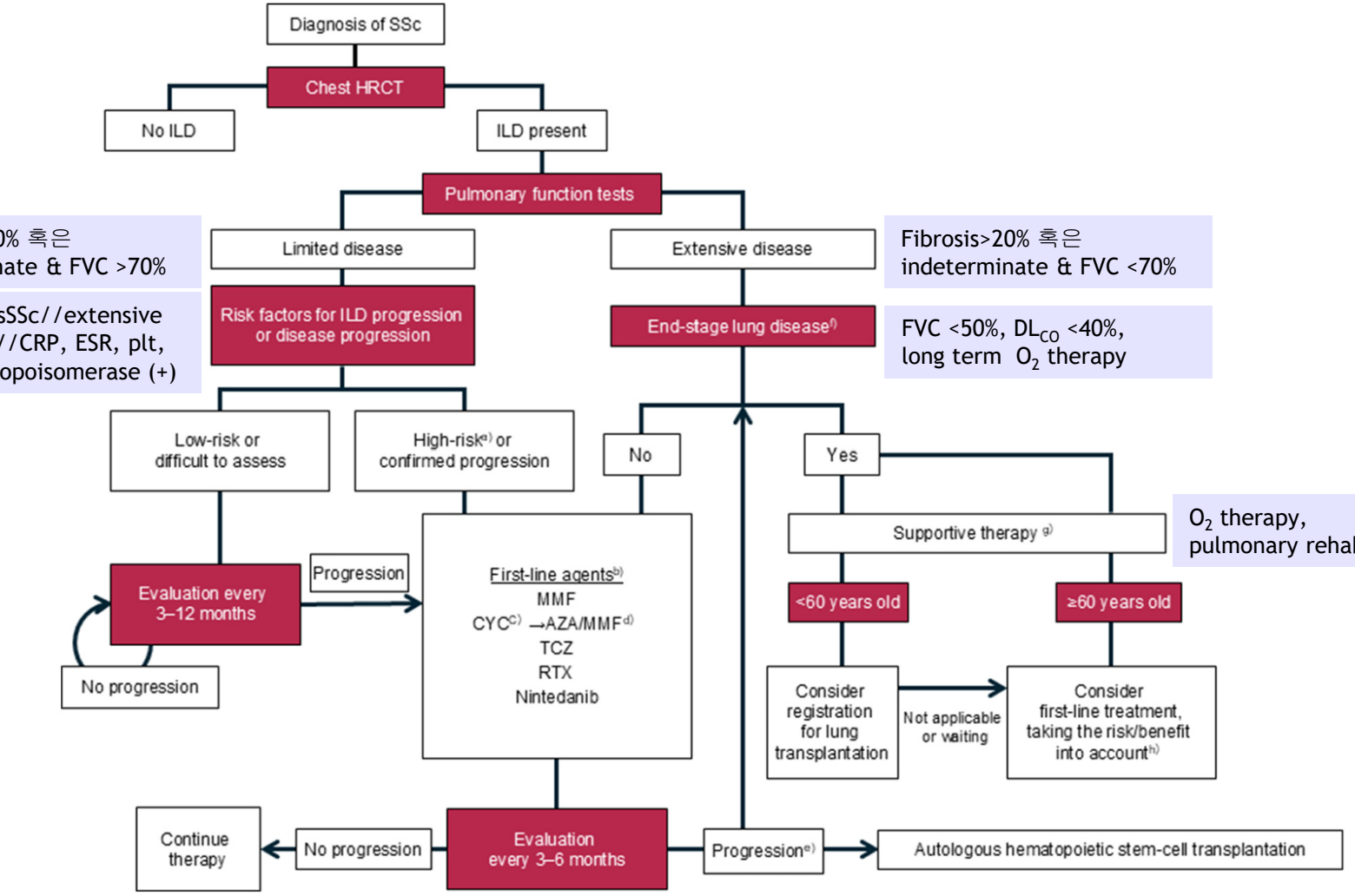

*Arthritis Rheumatol 2024; 76: 1201-1213*

# Treatment



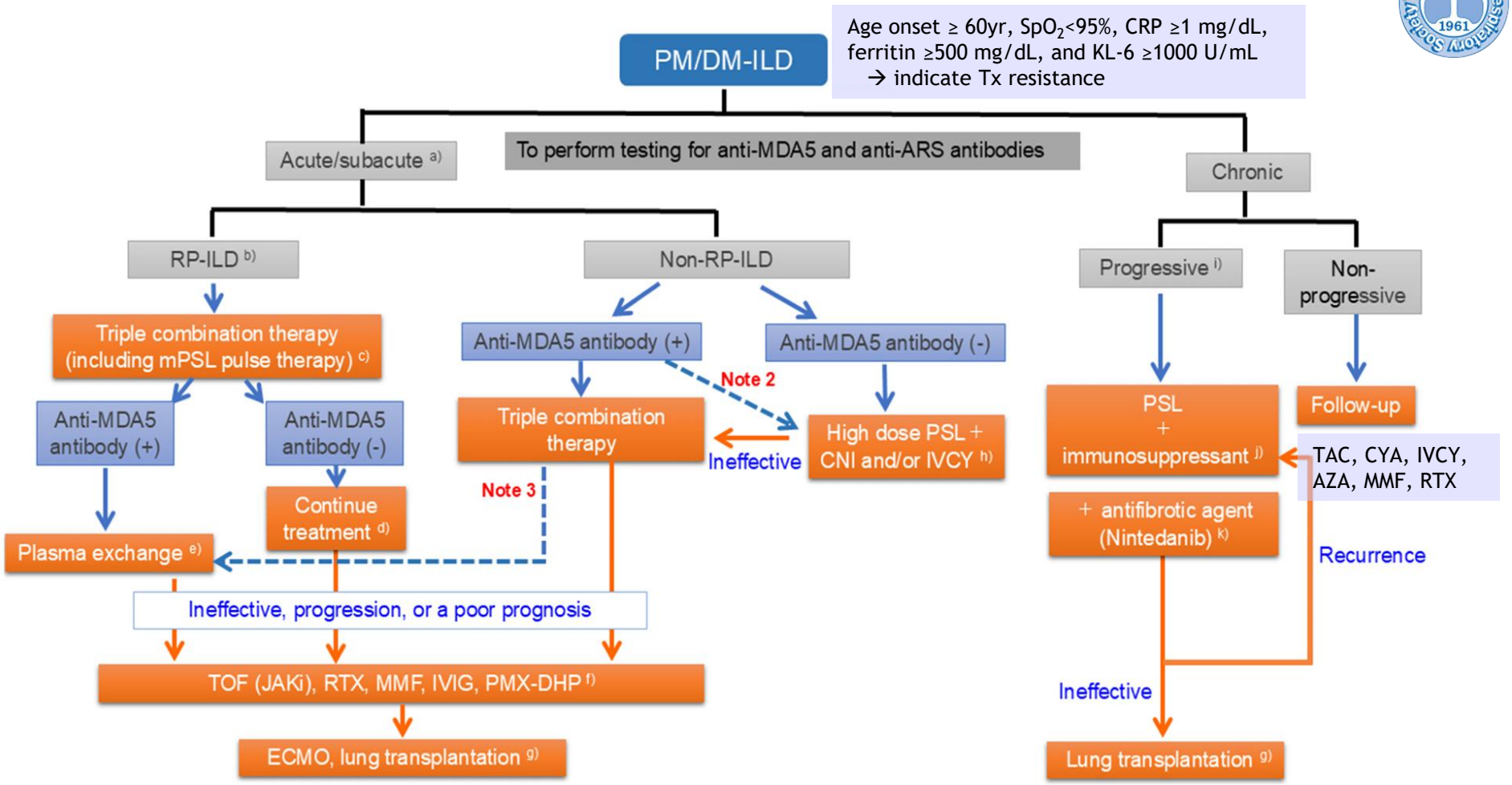

*Arthritis Rheumatol 2024; 76: 1201-1213*

# Treatment



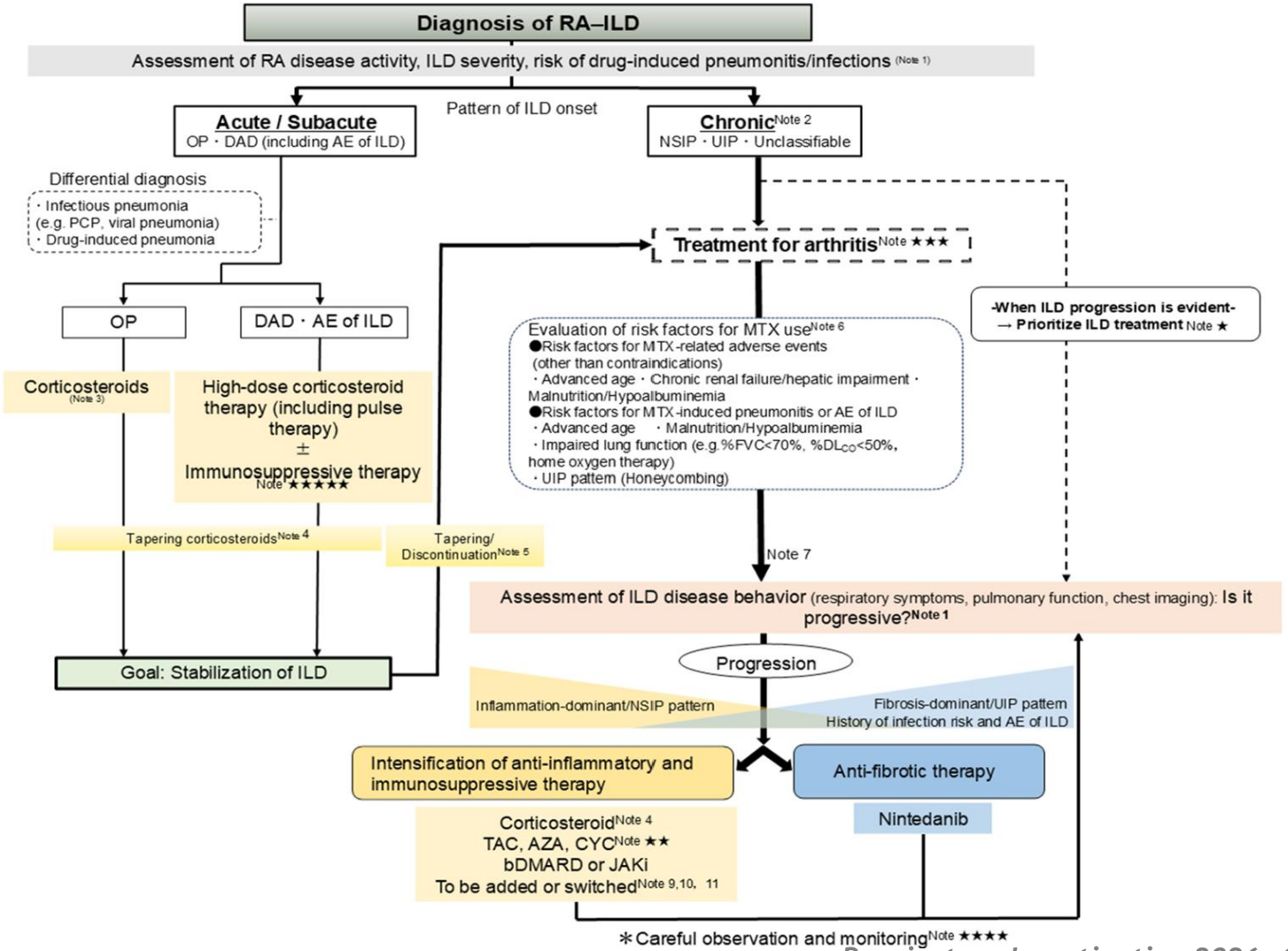

*Respiratory Investigation 2026; 64: 101412*

# Treatment




*Respiratory Investigation 2026; 64: 101412*

# Treatment




*Respiratory Investigation 2026; 64: 101412*

# Treatment

| 약 | 보험 기준 ( ILD) | 적용 날짜 |
|---|---|---|
| Cyclophosphamide(IV/PO) | DM/PM: Steroid 치료에 실패하였거나 투여가 불가능한 경우 | 2009.3.23 |
| MMF | DM/PM<br>CTD-ILD: 1종 이상의 타 면역억제제(AZA 등) 투여에도 불충분한 반응을 보이면서 45% ≤FVC <80%인 경우<br>SSc-ILD: : 1종 이상의 타 면역억제제(AZA 등) 투여에도 불충분한 반응을 보이면서 45% ≤ FVC <80%인 경우 | 2025.10.1<br>2024.4.1<br><br>2020.10.1 |
| Tacrolimus/Cyclosporin | DM/PM | 2025.10.1 |
| Rituximab, IVIG | DM/PM 중 가, 나, 다 모두 만족 시<br>가) 생검으로 증명된 DM/PM<br>나) 적어도 4-6개월 기존의 치료제(Steroid 등) 투여 후 부작용이 있거나 불응성인 중증 상태<br>다) 혈청 CK 의 지속적인 상승 | 2025.10.1 |
| Tofacitinib/tocilizumab | 허용 안 됨, only for RA | 현재 |
| Nintedanib | PPF 중 다음을 모두 만족 시<br>1) FVC ≥ 45%<br>2) 30% ≤ $DL_{CO}$ <80%<br>3) 기존 치료(steroid, 면역억제제 등)에도 불구하고 최근 24개월 이내 악화 확인 (FVC, 증상, CT 소견)<br>➔ 12개월 이내 FVC/CT 악화 시 투여 중단 | 2025.7.1 |
| Pirfenidone | 허용 안 됨 | 현재 |

# Summary (In my opinion)

**Monitoring**

**CXR, PFT, 6MWD**
**q 3~12m**

**HRCT ± KL-6**
**q 6~12 m**

Non RPILD

1st line
: Steroid (PO) ± AZA
Cyclophosphamide ± Steroid (SSc)
Steroid + Tacro/Cyclosporin/MMF (IIM)

Progression, lack of significant improvement, S/Ex

2nd line
: MMF, cyclophosphamide
Rituximab/IVIG (IIM)
Nintedanib (PPF)

Progression, lack of significant improvement, S/Ex

3rd line (허가 초가 혹은 RH 등과 협의)
: Pirfenidone(RA-UIP, PPF)
Tofacitinib (JAKi, IIM, RA)
Tocilizumab (SSc, RA)
Rituximab

RPILD

1st line
: IV Steroid pulse
+ IV Cyclophosphamide(max 6 month)
± Tacro/Cyclosporin (IIM)

2nd line
: Rituximab/IVIG (IIM)
MMF

3rd line (허가 초가 혹은 RH 등과 협의)
: Tofacitinib (JAKi, IIM, RA)
Plasmapheresis
ECMO, Lung transplantation

**Monitoring**

**CXR, PFT, 6MWD**
**HRCT ± KL-6**
**f/u at 3~6 m**

# Case 1 (F/48)

Myalgia, periorbital swelling, rash, cough, sputum

Dyspnea, fever

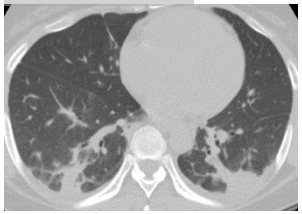
Dyspnea, fever, Well-being sense(-)

2025. 2.10(ER)

2025. 2.13(Adm)~2.28

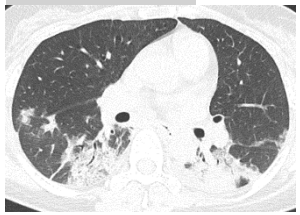
2025. 3.5(Adm)~5.2

2025. 2.10



Antibiotics

2025. 2.17

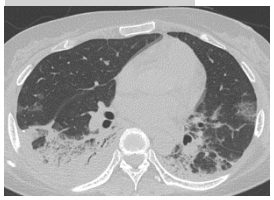


R/A: 96% (2.13)

AST/ALT 246/82
CPK 409, Aldolase 28, LDH 474
FANA(+),
SSA/B(+/+)
Jo-1(-), EMG(+)

VATS Bx(2.21)
: OP pattern
➔ Steroid 1mg/kg

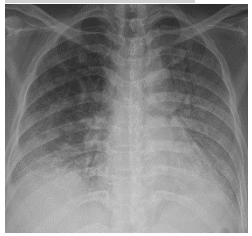
2025. 3.21



NP 1L : 94%
MDA 5 (+)

Steroid IV 1mg/kg
+ Azathioprine (3.5~)
⇒ Steroid pulse(3.21-23)
⇒ Rituximab
(비급여, 3.27)
➔ M enz & CXR 호전

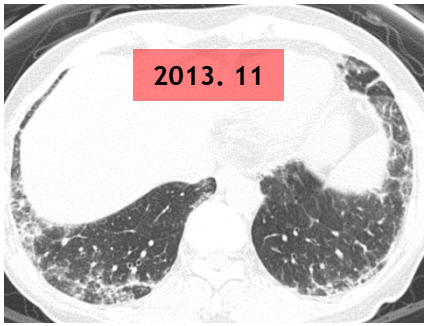
2025. 4.3



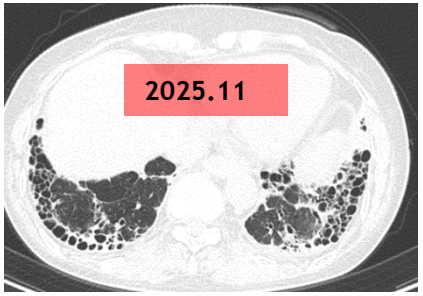
CXR 악화
Optiflow apply (4.3)
➔ PCP 의심하여
ICU 전실, intubation
PCP 치료 (4.4~)
➔ 호전 중 다시 악화
ECMO apply (4.9~)
➔ CMV 치료 (4.11~)
➔ Lung transplantation

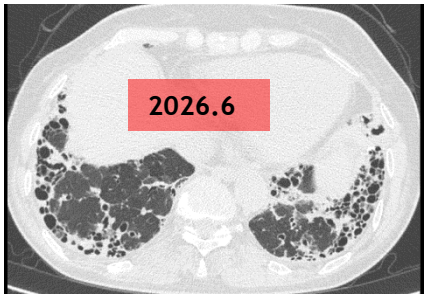
# Case 2 (F/73)

- 2013년 기침, 가래, 호흡곤란
  및 Chest CT에서 ILD 의심되어 내원
  ➔ VATS lung Bx(2013. 11)에서 NSIP pattern
  ➔ Sjögren's dz 진단, steroid 치료 후 f/u 중




| | FVC(%) | $DL_{CO}$ (%) |
|---|---|---|
| 2020.6 | 88 | 45 |
| 2023.9 | 81 | 43 |
| 2024.12 | 71 | 37 |
| 2025.11 | 59 | 38 |
| 2026.2 | 55 | 33 |
| 2026.6 | 70 | 40 |




Microscopic hematuria로 본원 신장내과에서 GN W/U 시행
➔ Kd Bx (2025.7)
: pauci-immune ANCA GN (microscopic polyarteritis)
➔ Steroid start (2025.8~)
➔ Proteinuria 증가
➔ Rituximab, 2025.11 (2회) 시행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