Δορυφορικό Συμπόσιο Boehringer Ingelheim

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Life forward

«Νέες κατευθυντήριες οδηγίες ERS/EULAR για την πνευμονική ίνωση σε ρευματικά νοσήματα»

Αργυρώ Ρέπα

Επιμελήτρια Α

Ρευματολογική κλινική ΠΑΓΝΗ

Ηράκλειο 29/6/2024

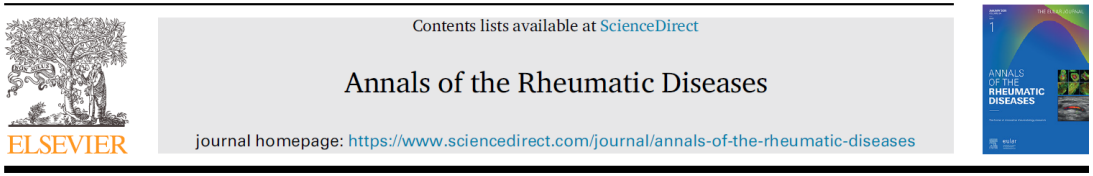
ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΝΟΣΟΚΟΜΕΙΟ ΗΡΑΚΛΕΙΟΥ

ΠΑΝΕΠΙΣΤΗΜΙΟ ΚΡΗΤΗΣ ΙΑΤΡΙΚΗ ΣΧΟΛΗ

Δήλωση σύγκρουσης συμφερόντων

- Τιμητική αμοιβή από την εταιρεία BOEHRINGER

Ann Rheum Dis 000 (2025) 1–39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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

- A collaborative effort
- Four disease groups:
  - Systemic sclerosis(SSc)
  - Idiopathic inflammatory myopathies(IIM)
  - OtherCTDs, including Sj€ogren disease(SjD), systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD)
  - Rheumatoid arthritis(RA) under the umbrella term CTD in this guideline.

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

	Recommendations		Strength of recommendation	Level/certainty of evidence
→	**Screening**			
	1) PICO 1–11	We recommend against replacing HRCT with pulmonary function tests for screening of ILD in patients with SSc, RA, IIM (S, L) and other CTDs (S, VL). We suggest not to replace HRCT with lung ultrasound for screening of ILD in patients with SSc, RA, IIM and other CTDs (C, L/VL).	S/C	L/VL
	2) NQ 1–5	We recommend that all patients with SSc and MCTD and IIM patients with risk factors should be screened (S, L); and suggest that all patients with RA and SjD with risk factors, and IIM patients without risk factors (C, L) could be screened for ILD.	S/C	L
→	**Diagnosis**			
	3) NQ 8–10	We suggest performing a global assessment of all risk factors of ILD progression in patients with SSc, RA and IIM to identify patients at higher risk of ILD progression and death.	C	L
	4) NQ 12–13	We suggest that BAL could be used in patients with any CTD-ILD at the time of diagnosis in cases where there is suspicion of infection or to exclude alternative diagnoses. We suggest that lung biopsy should not play a role for diagnosis.	C	VL
	5) NQ 14–19	We suggest using the 6MWT in patients without physical limitations and PROMs to assess severity and/or prognosis of ILD in any CTD-ILD patients.	C	L/VL
→	**Monitoring**			
	6) NQ 20–27	We suggest repeating PFTs every 3–6 months during the first years, and at least every 6–12 months thereafter. We suggest regularly repeating HRCT after 1–2 years in patients with SSc-ILD, RA-ILD and other CTD-ILD, and after 3–6 months in IIM-ILD, particularly in those at higher risk of progression. We suggest repeating PFTs and HRCT in case of suspected progression in any CTD-ILD patient.	C	L/VL
→	**Treatment**			
	7) PICO 12–15	We recommend using tocilizumab in a subgroup (S, M) and suggest using MMF, rituximab (C, VL), and cyclophosphamide (C, L) in patients with SSc-ILD.	S/C	M/L/VL
	8) PICO 16	We recommend using immunosuppressive treatment in patients with IIM-ILD.	S	VL
	9) PICO 17–18	We suggest using immunosuppressive treatment in patients with RA-, SjD-, MCTD- and SLE-ILD.	C	VL
	10) PICO 19–20	We suggest using nintedanib in SSc-ILD (C, M) and in any CTD-ILD (C, VL) patient with progressive pulmonary fibrosis.	C	M/L/VL
	11) PICO 21	We suggest using pirfenidone in patients with RA-ILD with a UIP pattern.	C	VL
	12) PICO 23	We suggest using combination therapy with nintedanib and MMF in patients with SSc-ILD.	C	VL
	13) PICO 24	We suggest using combination therapy with immunosuppressants including glucocorticoids in patients with IIM-ILD.	C	VL
	14) PICO 25	We suggest treating patients with any CTD-ILD with a combination of immunosuppressants or, in the presence of progressive pulmonary fibrosis, with a combination of an immunosuppressant and nintedanib.	C	VL
	15) NQ 28	We suggest using the inclusion criteria of RCTs to guide treatment decisions for CTD-ILD.	C	VL

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

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journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

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Screening			
1) PICO 1–11	We recommend against replacing HRCT with pulmonary function tests for screening of ILD in patients with SSc, RA, IIM (S, L) and other CTDs (S, VL). We suggest not to replace HRCT with lung ultrasound for screening of ILD in patients with SSc, RA, IIM and other CTDs (C, L/VL).	S/C	L/VL

- High likelihood of missing ILD if PFTs are used as the only screening tool.
- LUS :
  - False-negative /false-positive results
  - Very low certainty of evidence

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

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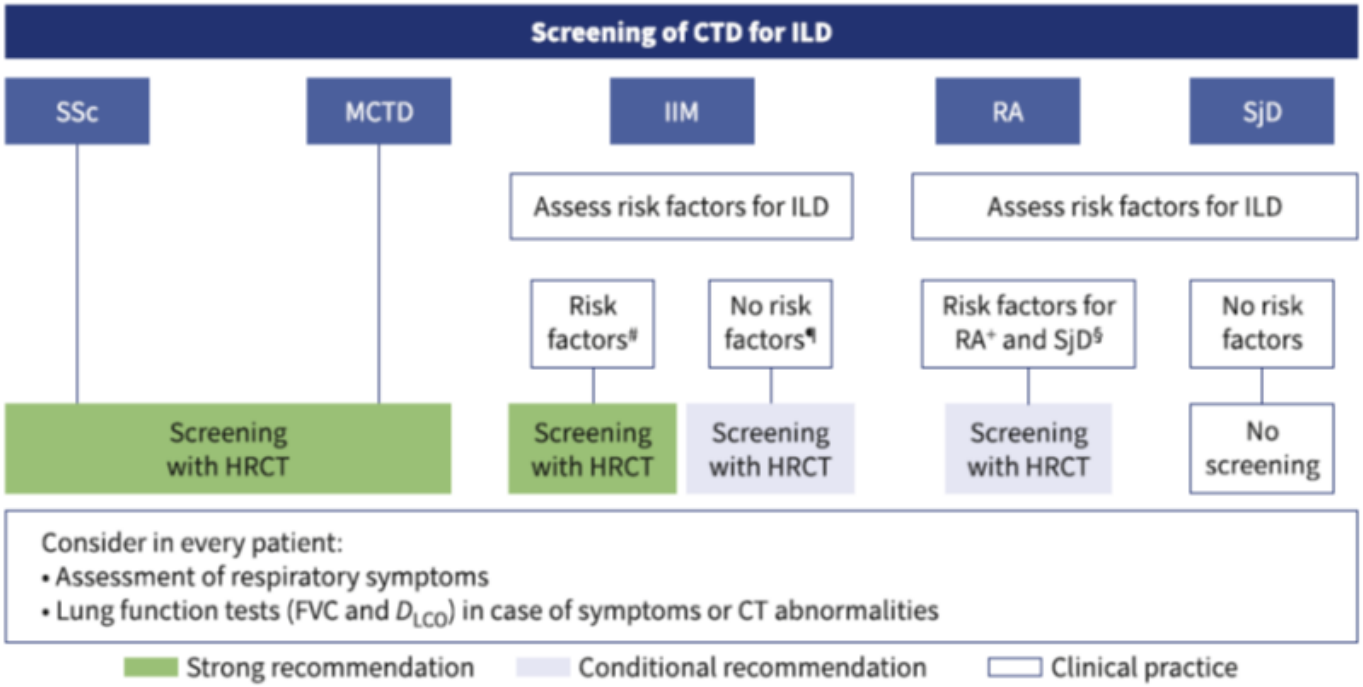

- No recommendation on how frequently patients with CTD should be screened for ILD.

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

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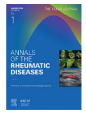

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

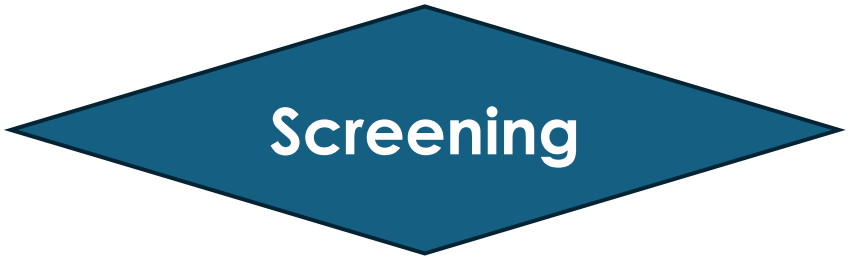

Table 3

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

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Diagnosis

Recommendations		Strength of recommendation	Level/certainty of evidence
Diagnosis			
3) NQ 8–10	We suggest performing a global assessment of all risk factors of ILD progression in patients with SSc, RA and IIM to identify patients at higher risk of ILD progression and death.	C	L
4) NQ 12–13	We suggest that BAL could be used in patients with any CTD-ILD at the time of diagnosis in cases where there is suspicion of infection or to exclude alternative diagnoses. We suggest that lung biopsy should not play a role for diagnosis.	C	VL
5) NQ 14–19	We suggest using the 6MWT in patients without physical limitations and PROMs to assess severity and/or prognosis of ILD in any CTD-ILD patients.	C	L/VL

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Diagnosis

SSc, RA, IIM, SjD, MCTD and SLE

ILD diagnosis

If alternative diagnosis or co-existing condition suspected

- Consider BAL
- Other tests for differential diagnoses

Assess prognosis, risk of progression and risk of development of severe disease

- Clinical risk factors#
- Lung function test (FVC and D_{LCO})#
- HRCT (pattern and extent)#
- 6MWT and O_2 desaturation#
- Patient-reported outcome measures

BAL with microbiology and cytology may be used to rule out infection, to diagnose some types of malignancy (*i.e.* low-grade lymphoma *e.g.* MALT lymphoma), and to exclude alveolar haemorrhage. Lung biopsy has no role in the diagnosis of ILD, but may be used when atypical features are identified on HRCT and/or to exclude malignancy.

Conditional recommendation Usual clinical practice

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Diagnosis

- **6MWT**

  - Predictor of respiratory deterioration and progression in patients with SSc-ILD
  - Predictor of mortality, acute respiratory deterioration and acute exacerbation inRA-ILD patients
  - Associated with ILD severity and worse prognosis in patients with other CTD-ILD.

  - Limited or no lower limb joint damage or active synovitis
  - Without significant muscle involvement of the lower limbs

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

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 • Male sex • African American ethnicity	• Older age at RA onset • Male sex	
Circulating markers	• Elevated ESR, CRP • ATA-I	• Anti-CCP, RF	• Elevated ferritin • 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 • 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	

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Monitoring

		Strength of recommendation	Level/certainty of evidence
6) NQ 20–27	We suggest repeating PFTs every 3–6 months during the first years, and at least every 6–12 months thereafter. We suggest regularly repeating HRCT after 1–2 years in patients with SSc-ILD, RA-ILD and other CTD-ILD, and after 3–6 months in IIM-ILD, particularly in those at higher risk of progression. We suggest repeating PFTs and HRCT in case of suspected progression in any CTD-ILD patient.	C	L/VL

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Monitoring

SSc-ILD monitoring

Assess prognosis, risk of progression and disease severity at every visit

	High risk		Low risk		Indication of progression
Disease duration	<3–5 years	>3–5 years	<3–5 years	>3–5 years	Anytime
Lung function test (FVC and D_{LCO})	Every 3–6 months	Every 6–12 months	Every 6–12 months	Every 12 months	Conduct
HRCT (pattern and extent)	Every 12 months	Every 12 months	After 2 years	Clinical indication	Conduct
6MWD and O_2 desaturation	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct
Patient-reported outcome measures	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct

Conditional recommendation Usual clinical practice

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Monitoring

RA-ILD monitoring

Assess prognosis, risk of progression and disease severity at every visit

	High risk		Low risk		Indication of progression
Disease duration	<1–2 years	>2 years	<1–2 years	>2 years	Anytime
Lung function test (FVC and D_{LCO})	Every 3–6 months	Every 6–12 months	Every 6–12 months	Every 12 months	Conduct
HRCT (pattern and extent)	Every 12 months	Every 12 months	After 2 years	Clinical indication	Conduct
6MWD and O_2 desaturation	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct
Patient-reported outcome measures	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct

Conditional recommendation Usual clinical practice

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Monitoring

IIM-ILD monitoring

Assess prognosis, risk of progression and disease severity at every visit

	High risk		Low risk		Indication of progression
Disease duration	<2 years	>2 years	<2 years	>2 years	Anytime
Lung function test (FVC and D_{LCO})	Every 3–6 months	Every 6–12 months	Every 6–12 months	Every 12 months	Conduct
HRCT (pattern and extent)	At every 3–6 months and every year	Every 12 months	Every year	Clinical indication	Conduct
6MWD and O_2 desaturation	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct
Patient-reported outcome measures	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct

Conditional recommendation Usual clinical practice

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Annals of the Rheumatic Diseases

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

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Other CTD-ILD (SjD, MCTD) monitoring

Assess prognosis, risk of progression and disease severity at every visit

	High risk		Low risk		Indication of progression
Disease duration	<1 year	>1 year	<1 year	>1 year	Anytime
Lung function test (FVC, FEV_1 and D_{LCO})	Every 3–6 months	Every 6–12 months	Every 6–12 months	Every 12 months	Conduct
HRCT (pattern and extent)	At 1 year	Every 12 months	At 1 year	Clinical indication	Conduct
6MWD and O_2 desaturation	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct
Patient-reported outcome measures	Every 6–12 months	Every 6–12 months	Every 12 months	Every 12 months	Conduct

Conditional recommendation Usual clinical practice

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

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Treatment			
7) PICO 12–15	We recommend using tocilizumab in a subgroup (S, M) and suggest using MMF, rituximab (C, VL), and cyclophosphamide (C, L) in patients with SSc-ILD.	S/C	M/L/VL
8) PICO 16	We recommend using immunosuppressive treatment in patients with IIM-ILD.	S	VL
9) PICO 17–18	We suggest using immunosuppressive treatment in patients with RA-, SjD-, MCTD- and SLE-ILD.	C	VL
10) PICO 19–20	We suggest using nintedanib in SSc-ILD (C, M) and in any CTD-ILD (C, VL) patient with progressive pulmonary fibrosis.	C	M/L/VL
11) PICO 21	We suggest using pirfenidone in patients with RA-ILD with a UIP pattern.	C	VL
12) PICO 23	We suggest using combination therapy with nintedanib and MMF in patients with SSc-ILD.	C	VL
13) PICO 24	We suggest using combination therapy with immunosuppressants including glucocorticoids in patients with IIM-ILD.	C	VL
14) PICO 25	We suggest treating patients with any CTD-ILD with a combination of immunosuppressants or, in the presence of progressive pulmonary fibrosis, with a combination of an immunosuppressant and nintedanib.	C	VL
15) NQ 28	We suggest using the inclusion criteria of RCTs to guide treatment decisions for CTD-ILD.	C	VL

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

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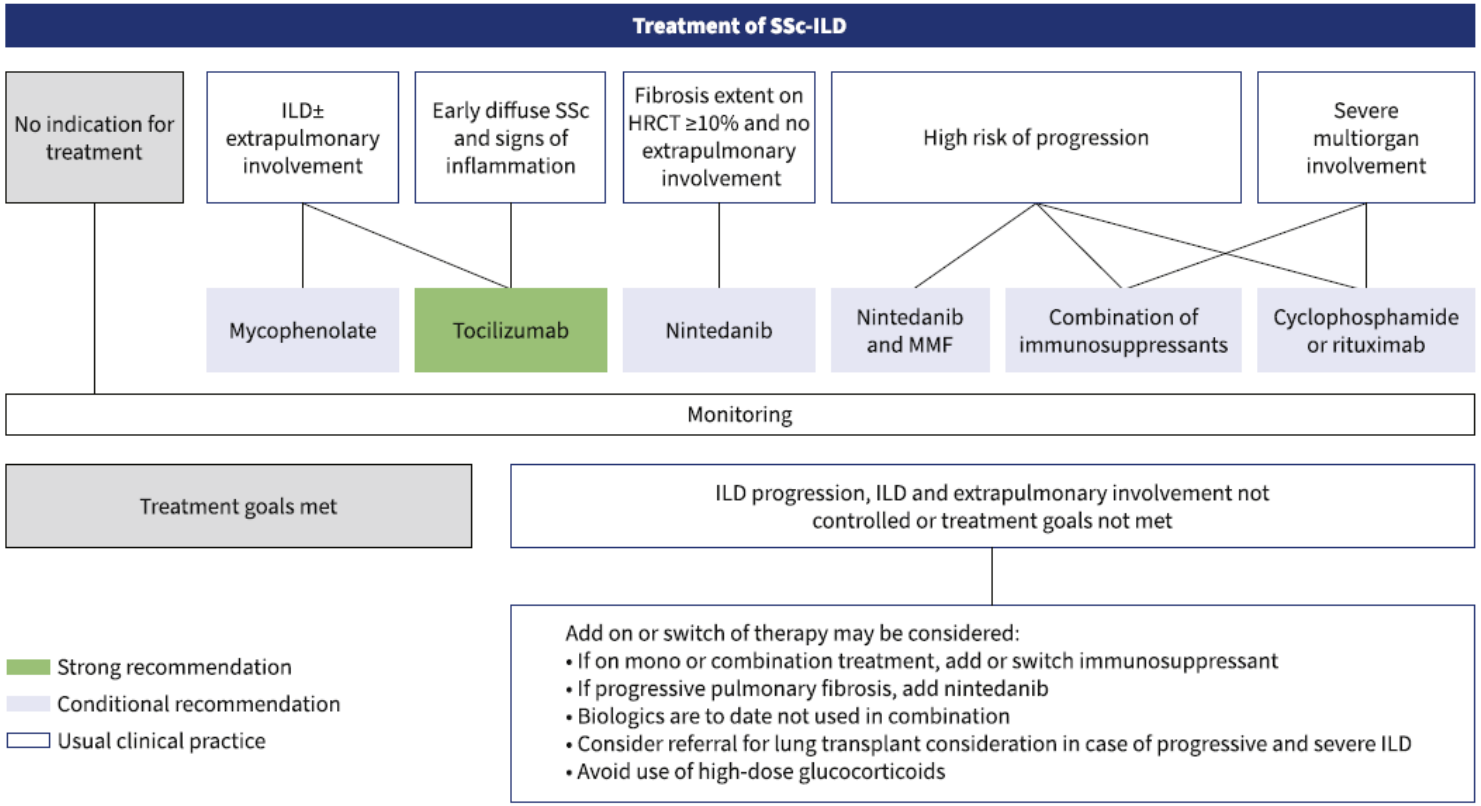

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

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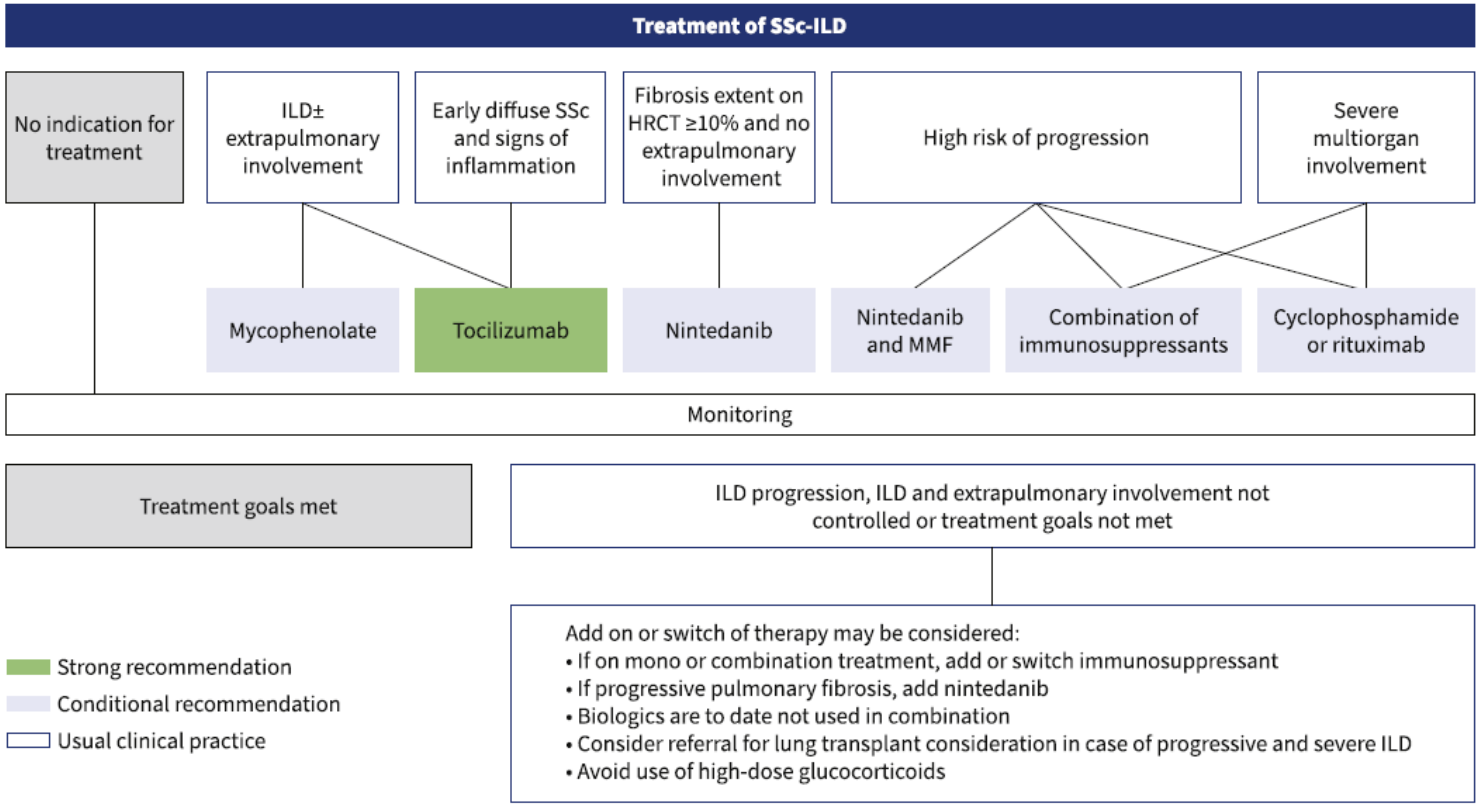

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

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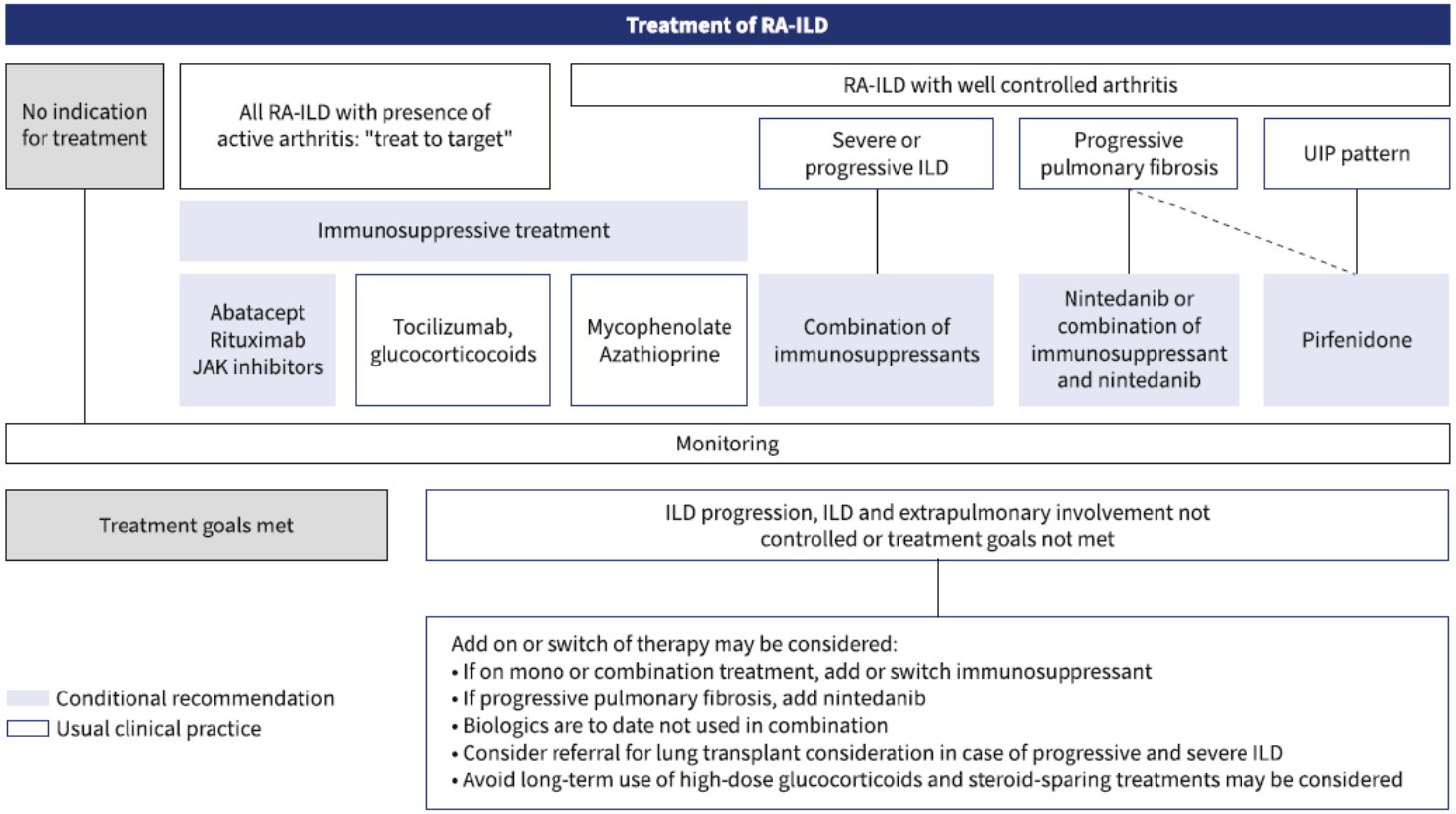

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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Version of Record

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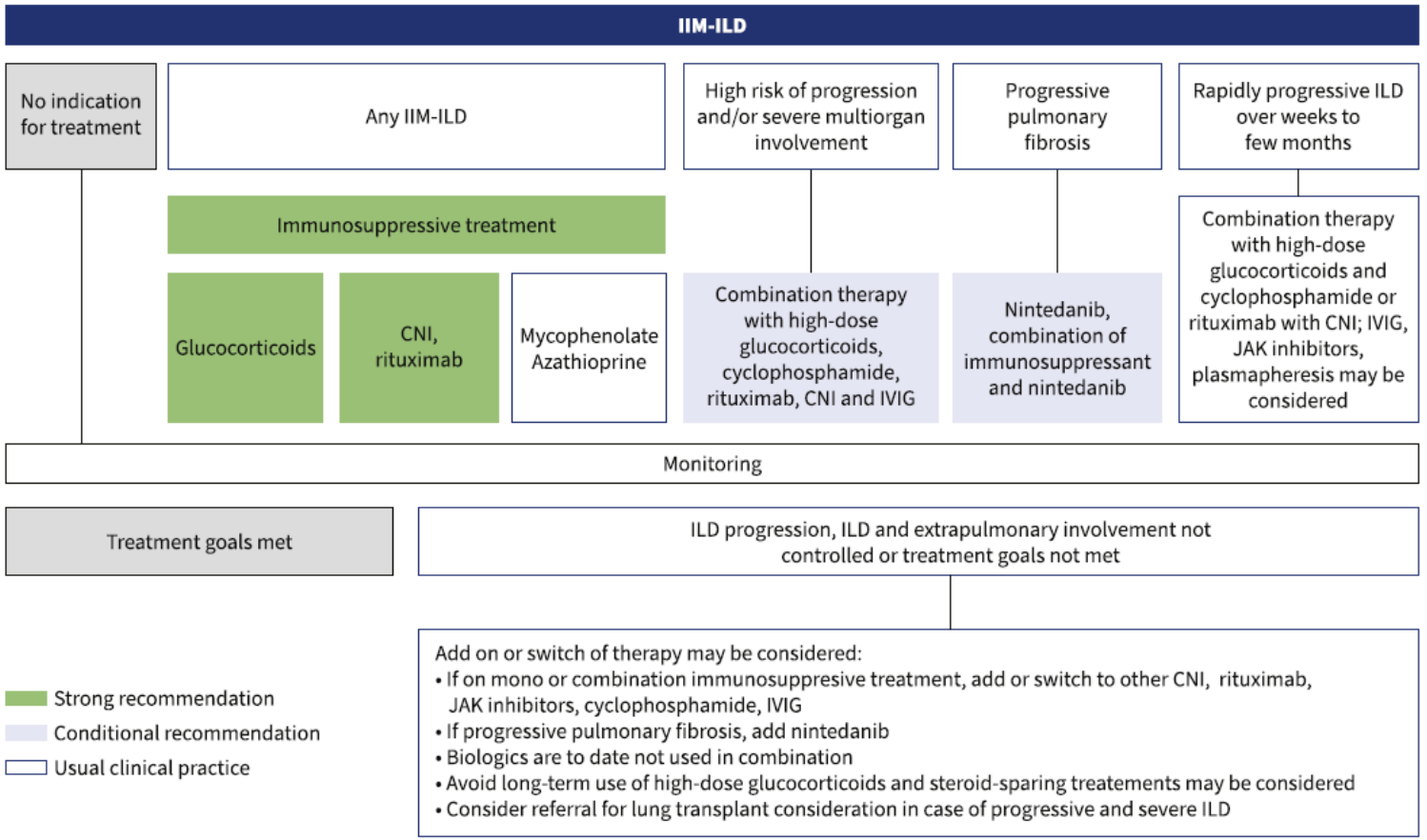

K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

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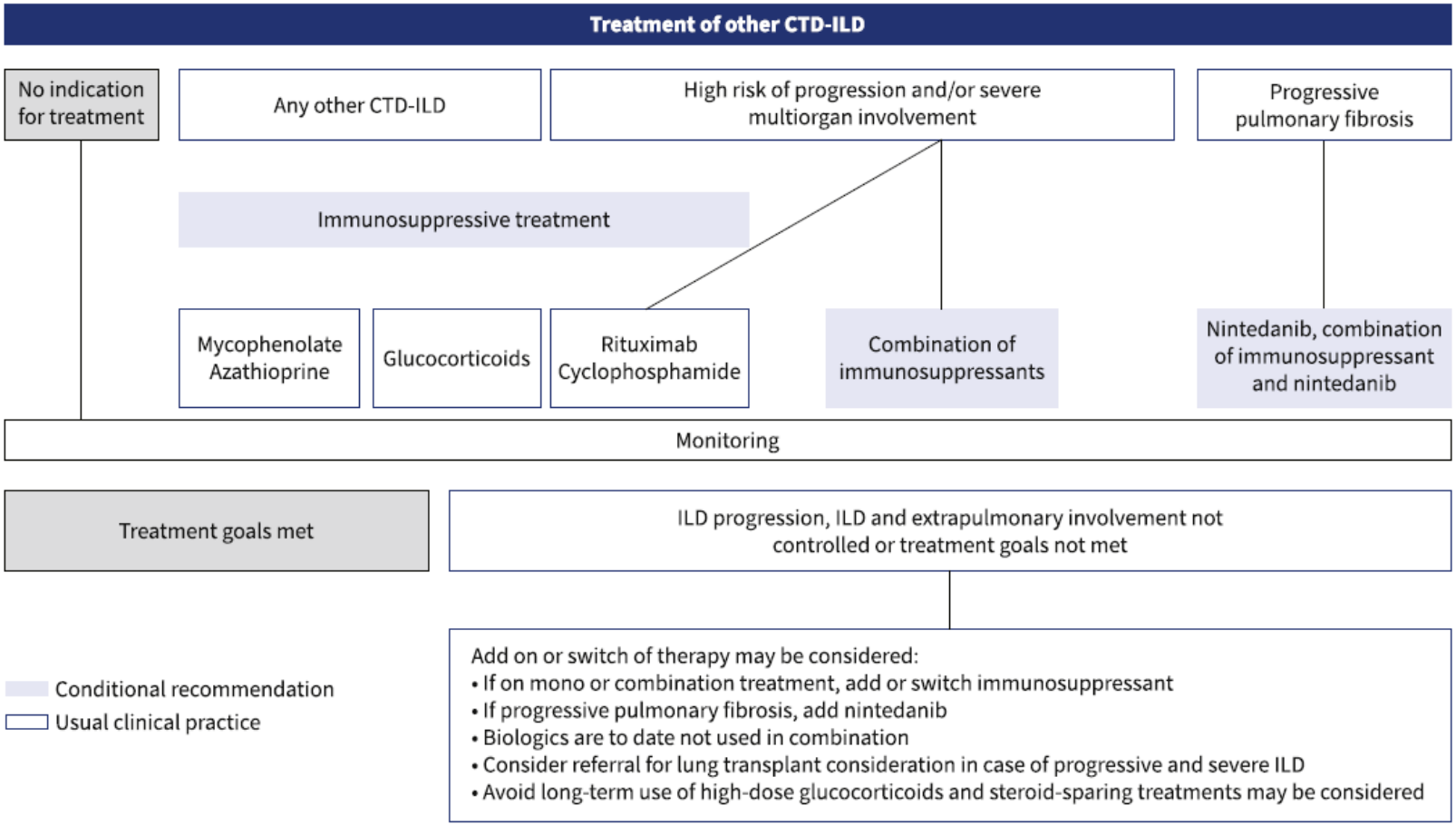
Treatment

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease



K.M. Antoniou et al. Ann Rheum Dis(2025)

Ann Rheum Dis 000 (2025) 1–39

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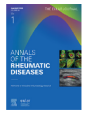

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

- Low and very low certainty evidence
- Conditional recommendations
- Studies needed

K.M. Antoniou et al. Ann Rheum Dis(2025)