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

Guideline Summary

This guideline provides evidence-based recommendations for the treatment of Interstitial Lung Disease (ILD) in adults with Systemic Autoimmune Rheumatic Diseases (SARDs) at greatest risk of ILD, including systemic sclerosis (SSc), rheumatoid arthritis (RA), idiopathic inflammatory myopathies (IIM including polymyositis, dermatomyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy), mixed connective tissue disease (MCTD), and Sjögren's Disease (SjD). This document summarizes 36 treatment recommendations for first-line ILD treatment, treatment for ILD progression despite first-line treatment, and treatment of Rapidly Progressive ILD (RP-ILD).

Table 1. Summary of Recommendations for Management of SARD-ILD: First-line ILD Treatment

Recommendations
For people with SARD-ILD other than SSc-ILD, we **conditionally** recommend glucocorticoids as a first-line ILD treatment.
For people with SSc-ILD, we **strongly** recommend *against* glucocorticoids as a first-line ILD treatment.
For people with SARD-ILD, we **conditionally** recommend mycophenolate, azathioprine, rituximab, and cyclophosphamide as first-line ILD treatment options.
For people with SSc-ILD and MCTD-ILD, we **conditionally** recommend tocilizumab as a first-line ILD treatment option.
For people with SARD-ILD, we **conditionally** recommend *against* leflunomide, methotrexate, TNFi, and abatacept as first-line ILD treatment options.
For people with SjD-ILD, IIM-ILD, and MCTD-ILD, we **conditionally** recommend *against* nintedanib as a first-line ILD treatment option.
For people with SSc-ILD, we **conditionally** recommend nintedanib as a first-line ILD treatment option.
For people with RA-ILD, the Panel was not able to come to consensus on whether to recommend nintedanib as a first-line ILD treatment option.

For people with SARD-ILD, we **conditionally** recommend *against* pirfenidone as a first-line ILD treatment option.
For people with SARD-ILD receiving mycophenolate without evidence of ILD progression, we **conditionally** recommend *against* adding nintedanib or pirfenidone to mycophenolate.
For people with SARD-ILD, we **conditionally** recommend *against* upfront combination of nintedanib or pirfenidone with mycophenolate over mycophenolate alone as first-line ILD treatment options.
For people with IIM-ILD, we **conditionally** recommend JAK inhibitors as a first-line ILD treatment option.
For people with SARD-ILD other than IIM-ILD, we **conditionally** recommend *against* JAK inhibitors as a first-line ILD treatment option.
For people with IIM-ILD, we **conditionally** recommend CNI as a first-line ILD treatment option.
For people with SARD-ILD other than IIM-ILD, we **conditionally** recommend *against* CNI as a first-line ILD treatment option.
For people with SARD-ILD, we **conditionally** recommend *against* IVIG or plasma exchange as first-line ILD treatment options.
For people with SARD-associated ILD, we **conditionally** recommend optimal medical management over referral for stem cell or lung transplant as first-line ILD treatment options.

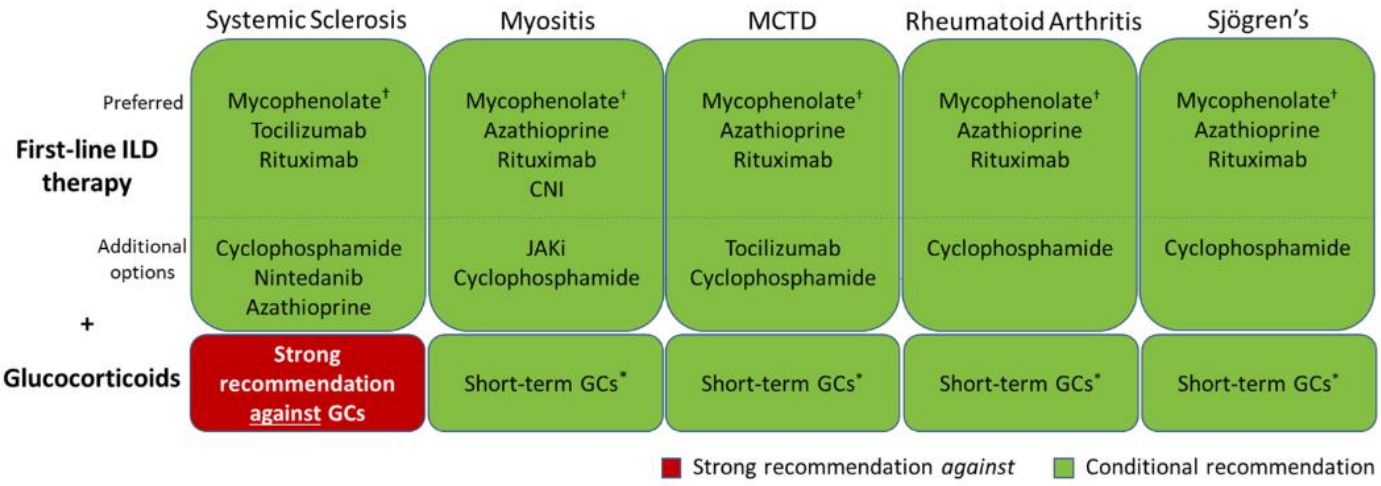
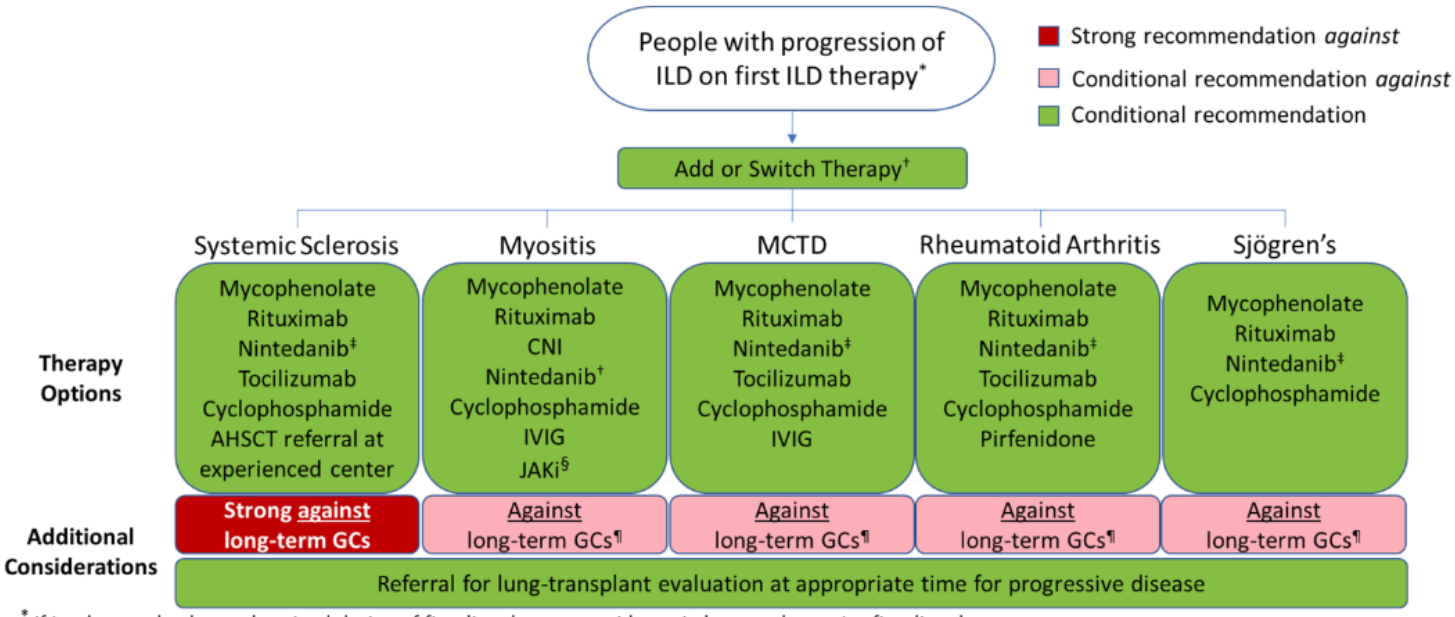


Figure 1: Initial treatment options for the treatment of interstitial lung disease associated with systemic autoimmune rheumatic diseases of interest.
* Decisions on GC dose and use of oral versus intravenous therapy depend on severity of disease. GCs should be used cautiously in patients with MCTD with a systemic sclerosis phenotype who may be at increased risk of renal crisis.
† Treatments are listed in order based on a hierarchy established by head-to-head votes, although the panel noted that decisions on which first-line therapy to use were dependent on specific situations and patient factors. In all diseases, mycophenolate was conditionally recommended over the other listed therapies. Therapies here are divided into "preferred" options and "additional options" based on the rank-order hierarchy.
MCTD = mixed connective tissue disease; GCs = glucocorticoids; CNI = calcineurin inhibitor; JAKi = janus kinase inhibitor

Figure 1. Recommendations for Management of SARD-ILD: First-line ILD Treatment

Table 2. Recommendations for Management of SARD-ILD Progression Despite First-line ILD Treatment

Recommendations
For people with SSc-ILD progression despite first ILD treatment, we **strongly** recommend *against* using long-term glucocorticoids, and in other SARD-ILD we **conditionally** recommend *against* using long-term glucocorticoids.
For people with SARD-ILD progression despite first ILD treatment, we **conditionally** recommend mycophenolate, rituximab, cyclophosphamide, and nintedanib as treatment options.
For people with RA-ILD progression despite first ILD treatment, we **conditionally** recommend adding pirfenidone as a treatment option.
For people with SARD-ILD, other than RA-ILD, progression despite first ILD treatment, we **conditionally** recommend *against* adding pirfenidone as a treatment option.
For people with SSc-ILD, MCTD-ILD, and RA-ILD progression despite first ILD treatment, we **conditionally** recommend using tocilizumab as a treatment option.
For people with SjD-ILD and IIM-ILD progression despite first ILD treatment, we **conditionally** recommend *against* using tocilizumab as a treatment option.
For people with IIM-ILD progression despite first ILD treatments, we **conditionally** recommend using a calcineurin inhibitor as a treatment option.
For people with SARD-ILD, other than IIM-ILD, progression despite first ILD treatments, we **conditionally** recommend *against* using a calcineurin inhibitor as a treatment option.
For people with IIM-ILD progression despite first ILD treatment, we **conditionally** recommend using JAK inhibitors as a treatment option.
For people with IIM-ILD and MCTD-ILD progression despite first ILD treatment, we **conditionally** recommend adding IVIG as a treatment option.
For people with SARD-ILD progression despite first ILD treatment, we **conditionally** recommend *against* using plasma exchange as a treatment option.
For people with SSc-ILD progression despite first ILD treatment, we **conditionally** recommend referral for stem cell transplantation and/or lung transplantation.



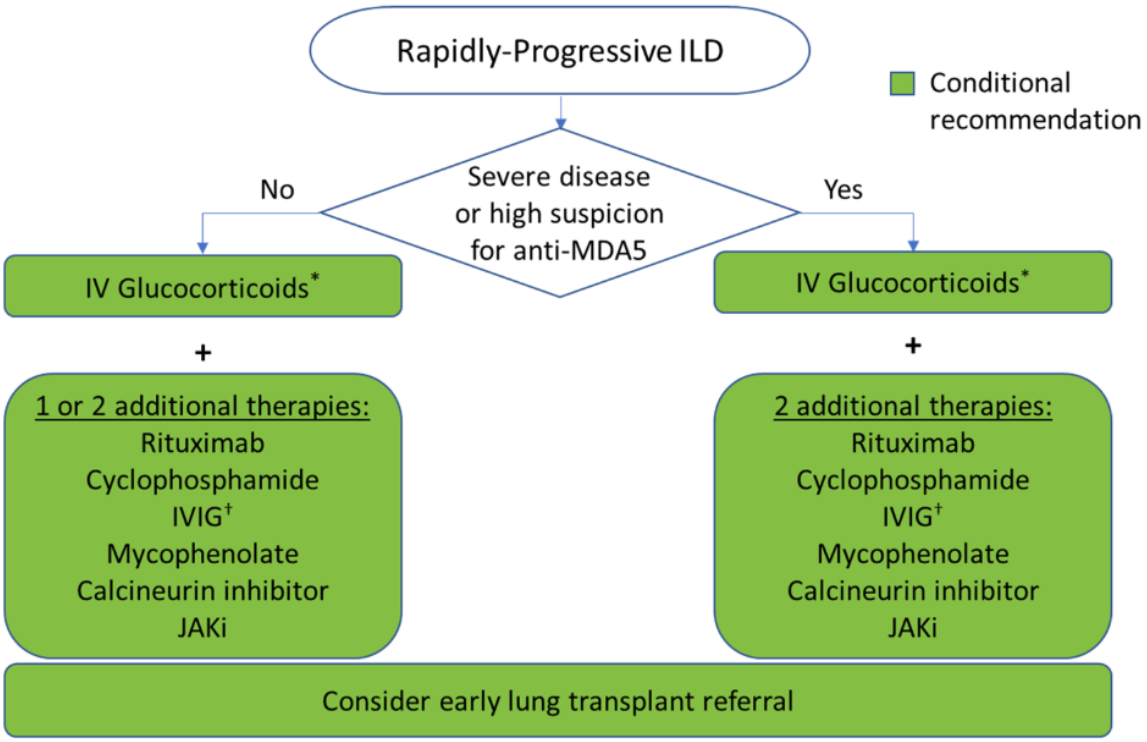
* If intolerance leads to suboptimal dosing of first-line therapy consider switch to an alternative first-line therapy.
† Therapies are generally listed in order based on a hierarchy established by head-to-head votes, but decisions depend on specific clinical situations. Decision on whether to switch therapy or add to current therapy depends on current therapy and on which therapy is being initiated. Cyclophosphamide is not typically used in combination with other therapies, while others may be used individually or in combination.
‡ Decision on use of nintedanib vs immunosuppression depends on pace of progression and amount of fibrotic disease or presence of a usual interstitial pneumonia pattern on CT chest.
§ JAKi conditionally recommended as an option particularly in patients with anti-MDA-5.
¶ Short-term glucocorticoids may be of use in some patients with disease flares or as a bridge when switching therapy
MCTD = mixed connective tissue disease; CNI = calcineurin inhibitor; AHSCT = autologous hematopoetic stem cell transplant; GCs = glucocorticoids

Figure 2. Recommendations for Management of SARD-ILD Progression Despite First-line ILD Treatment

Table 3. Recommendations for Management of SARD with Rapidly Progressive ILD (RP-ILD)

Recommendations
For people with SARD and RP-ILD, we **conditionally** recommend pulse intravenous methylprednisolone as a first-line RP-ILD treatment.
For people with SARD and RP-ILD, we **conditionally** recommend rituximab, cyclophosphamide, IVIG, mycophenolate, CNI, and JAK inhibitors as first-line RP-ILD treatment options.
For people with SARD and RP-ILD, we **conditionally** recommend *against* methotrexate, leflunomide, azathioprine, TNF inhibitors, abatacept, tocilizumab, nintedanib, pirfenidone, and plasma exchange as first-line RP-ILD treatment options.

For people with RP-ILD, we **conditionally** recommend up-front combination therapy (triple therapy for those with confirmed or suspected MDA-5 and double or triple therapy for those without confirmed or suspected MDA-5) over monotherapy as first-line treatment
For people with SARD and RP-ILD, we **conditionally** recommend *against* referral for stem cell transplantation over optimal medical management as a first-line RP-ILD treatment.
For people with SARD and RP-ILD, we **conditionally** recommend early referral for lung transplantation over later referral after progression on optimal medical management.



* In rare patients with systemic sclerosis with rapidly progressive ILD, there was no consensus on whether or not to use glucocorticoids – if used, patients should be monitored closely for evidence of renal crisis.
† Rituximab and cyclophosphamide recommended over IVIG, but IVIG may be preferred if there is high concern for infection.
ILD = interstitial lung disease; IV = intravenous; IVIG = intravenous immune globulin; JAKi = janus kinase inhibitor

Figure 3. Recommendations for Management of SARD with Rapidly progressive ILD (RP-ILD)

This summary was approved by the ACR Board of Directors on 12 August 2023. These recommendations are included in a full manuscript, pending peer review, which was submitted for publication in Arthritis & Rheumatology and Arthritis Care and Research.