AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

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

Project Plan – August 2022

PARTICIPANTS

Core Oversight Team

Sindhu R. Johnson, MD, PhD (Co-principal Investigator)
Elana J. Bernstein, MD, MSc (Co-principal Investigator)
Marcy B. Bolster, MD (Content Expert)
Jonathan H. Chung, MD (Content Expert)
Sonye Danoff, MD, PhD (Content Expert)
Michael George, MD, MSCE (Content Expert)
Dinesh Khanna, MD, MS (Content Expert)
Ilya Ivlev, MD, PhD, MBI (Co-Literature Review Leader)
Stacey Uhl (Co-Literature Review Leader)
Gordon Guyatt, MD (GRADE Expert)
Reza Mirza, MD (GRADE/Methodological Contributor)

Literature Review Team

Sandeep Agarwal, MD, PhD
Danielle Antin-Ozerkis, MD
Bradford Bemiss, MD
Vaidehi Chowdhary, MBBS, MD, DM
Jane E. Dematte D'Amico, MD
Robert Hallowell, MD
Alicia M. Hinze, MD, MHS
Patil A. Injean, DO
Nikhil Jiwrajka, MD
Elena Joerns, MD
Joyce Lee, MD
Ashima Makol, MD
Gregory McDermott, MD
Jake G Natalini, MD
Justin Oldham, MD, MS
Didem Saygin, MD
Kimberly Showalter Lakin, MD, MS
Namrata Singh, MD, MSCI
Joshua J. Solomon, MD
Jeffrey Sparks, MD, MMSc
Marat Turgunbaev, MD, MPH
Samera Vaseer, MD

ACR Board Liaison

Marcy B. Bolster, MD

Voting Panel

Rohit Aggarwal, MD, MS
Shervin Assassi, MD, MS
Lenore Buckley, MD, MPH
Paul F. Dellaripa, MD
Robyn T. Domsic, MD, MPH
Tracy Doyle, MD
Tracy M. Frech, MD, MS
Monique E. Hinchcliff, MD, MS
Cheilonda Johnson, MD, MHS
Jeffrey P. Kanne, MD
John S. Kim, MD
Scott Matson, MD
Zsuzsanna McMahan, MD, MHS
Lee Shapiro, MD
Christine D. Sharkey, MD
Ross S. Summer, MD
John Varga, MD

Patient Panel

TBD

ACR Staff

Cindy Force
Regina Parker
Amy Turner

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

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

Project Plan – August 2022

ORGANIZATIONAL LEADERSHIP AND SUPPORT

This project is led and funded by the American College of Rheumatology (ACR).

BACKGROUND

Interstitial lung disease (ILD), a heterogeneous group of disorders characterized by inflammation and fibrosis of the lung parenchyma, is a significant cause of morbidity and mortality in people with systemic autoimmune rheumatic diseases (ARDs). Although all people with ARDs are at risk for developing ILD, those with systemic sclerosis (SSc), rheumatoid arthritis (RA), mixed connective tissue disease (MCTD), polymyositis/dermatomyositis (PM/DM), and Sjogren's Syndrome (SS) are at the greatest risk (1,2) For example, ILD affects approximately 40-60% of adults with SSc and is the leading cause of death and hospitalization in this population (3-6).

Despite the life-threatening nature of ARD-ILD and the emerging potential of new therapies to arrest disease progression, there are no clinical practice guidelines for ILD screening or treatment in the ARDs. It is hypothesized that screening for ARD-ILD could lead to early interventions to prevent or slow progression of this often lethal disease. Hence, there is an urgent need to develop ARD-ILD screening, monitoring, and treatment guidelines.

OBJECTIVES

The objective of this project is to develop a clinical practice guideline that includes evidence-based consensus recommendations for clinicians who care for people with systemic autoimmune rheumatic disease who are at risk for or have been diagnosed with interstitial lung disease (ILD).

Specifically, we aim to:

1. Develop recommendations regarding optimal screening tests to screen for ILD in people with specific ARDs.
2. Develop recommendations for the monitoring of ARD-ILD (monitoring for both the development and progression of ARD-ILD).
3. Develop treatment recommendations for ARD-ILD.

THEMES OF PICO QUESTIONS

The PICO (Population/patients, Intervention, Comparator, and Outcomes; *see Appendix A*) questions developed for this guideline fall into 5 major categories:

1. Screening for ILD in people with rheumatic disease at increased risk of developing ILD
2. Monitoring ILD progression and treatment complications
3. Treatment of ILD: first therapy
4. Treatment of ILD after ILD progression on first ILD therapy
5. Treatment of rapidly progressive ILD

METHODS

Identification of Studies

Literature search strategies, based on PICO questions, were drafted by a research librarian with input from the Core Team. Searches were performed in OVID Medline (1946 +), Embase (1974 +), and PubMed (mid-1960s +).

The search strategies were developed using the controlled vocabulary or thesauri language for each database: Medical Subject Headings (MeSH) for OVID Medline and PubMed; and Emtree terms for Embase. Text words were also used in OVID Medline, PubMed, and Embase.

Search Limits

Only English language articles will be retrieved.

Literature Search Update

Literature searches will be updated just before the voting panel meeting to ensure completeness.

Inclusion/Exclusion Criteria

Appendix A includes the project's PICO questions, which outline the defined patient population, interventions, comparators, and outcomes. *Appendix B* includes the list of inclusion/exclusion criteria.

Management of Studies and Data

References and abstracts will be imported into bibliographic management software (EndNote) (7), duplicates removed, and exported to Distiller SR, a web-based systematic review manager (8). Screening and data abstraction forms will be created in Distiller SR. Search results will be divided among reviewers, and two reviewers will screen each title/abstract, with disagreements at the title/abstract screening stage defaulting to inclusion for full manuscript review. Following the same dual review process, disagreements at the full manuscript screening stage will be discussed and adjudicated by the literature review leadership, if necessary.

Phases

1. A search for randomized controlled trials and observational studies will be performed to determine existing studies covering outcomes of interest.

2. Additionally, recently published systematic reviews covering outcomes of interest will also be sought and used for reference cross-checking.
3. Chosen studies will be quality-assessed using the Instrument to assess the Credibility of Effect Modification Analyses.
4. Subsequently, identified studies will be assessed using the RevMan (10) and GRADE Pro tools (11).

GRADE Methodology

GRADE methodology will be used in this project to grade available evidence and facilitate development of recommendations. The certainty in the evidence (also known as 'quality' of evidence) will be graded as high, moderate, low or very low. The recommendations will have a strength, strong or conditional, and a direction, as in favor of or against the intervention. The strength of recommendations will not depend solely on the certainty in the evidence, but also on patient preferences and values, and the weight between benefits and harms. A series of articles that describe the GRADE methodology can be found on the GRADE working group's website: www.gradeworkinggroup.org.

Data Analysis and Synthesis

The literature review team will analyze and synthesize data from included studies that address the PICO questions. An evidence profile, including a GRADE Summary of Findings table, will be prepared for each PICO question using Review Manager (RevMan) (10) and GRADEprofiler (GRADEpro) software (11). The Summary of Findings table contains the benefits and harms for each outcome across studies, the assumed and corresponding risk for comparators and interventions (95% CI), the absolute risk and relative effect (95% CI), the number of participants/number of studies, and the certainty in the evidence for each critical and important outcome (i.e., high, moderate, low or very low).

The evidence profile documents the overall certainty in the evidence for each critical and important outcome across studies and summarizes the rationale of the GRADE criteria for downgrading (risk of bias, inconsistency, indirectness, imprecision, and publication bias), or upgrading the certainty in a body of evidence (large magnitude of effect, dose-response gradient, and all plausible confounding that would reduce a demonstrated effect).

Development of Recommendation Statements

PICO questions will be revised into drafted recommendation statements. Using the GRADE Evidence Profiles and Summaries of Findings tables, the voting panel, consisting of 11 rheumatologists, 5 pulmonologists, 1 radiologist, and at least 2 patients with rheumatic disease-associated ILD (specifically, ILD associated with either systemic sclerosis, rheumatoid arthritis, mixed connective tissue disease, dermatomyositis, polymyositis, or Sjogren's syndrome), will consider the drafted recommendation statements in two stages. The first assessment will be done individually, and the results will be

anonymous; this vote will only be used to determine where consensus might or might not already exist and develop an agenda for a virtual voting panel meeting. At the virtual voting panel meeting, chaired by the principal investigators, the panelists will discuss the evidence in the context of their clinical experience and expertise to arrive at consensus on the final recommendations. The voting panel meeting discussions will be supported by the GRADE expert as well as the literature review leader, who will attend the meeting to provide details about the evidence, as requested. Voting panel discussions and decisions will also be informed by a separately convened patient panel, which will meet in the days before the voting panel meeting, to provide unique patient perspectives on the drafted recommendations based on their experiences and the available literature.

PLANNED APPENDICES (AT MINIMUM)

A. Final literature search strategies
B. Inclusion/exclusion criteria
C. GRADE evidence profiles and summary of findings tables for each PICO question

AUTHORSHIP

Authorship of the guideline will include co-principal investigators Sindhu R. Johnson, MD, PhD, and Elana J. Bernstein, MD, MSc; co-literature review leaders Ilya Ivlev, MD, PhD, MBI and Stacey Uhl; MS content experts Marcy B. Bolster, MD, Jonathan H. Chung, MD, Sonye Danoff, MD, PhD, Michael George, MD, MSCE, and Dinesh Khanna, MD; and Gordon Guyatt, MD, GRADE expert, and Reza Mirza, MD, GRADE/Methodological Contributor. Members of the voting panel and literature review team will also be authors. The PIs will determine final authorship, dependent on the efforts made by individuals throughout the guideline development process, using international authorship standards as guidance.

DISCLOSURES/CONFLICTS OF INTEREST

The ACR's disclosure and COI policies for guideline development will be followed for this project. These can be found in the ACR Guideline Manual on this page of the ACR web site, under Policies & Procedures. *See Appendix D for participant disclosures.*

REFERENCES

1. Fischer A, Strek ME, Cottin V, et al. Proceedings of the American College of Rheumatology/Association of Physicians of Great Britain and Ireland Connective Tissue Disease-Associated Interstitial Lung Disease Summit: A Multidisciplinary Approach to Address Challenges and Opportunities. Arthritis & rheumatology 2019;71:182-95.

2. Fischer A, du Bois R. Interstitial lung disease in connective tissue disorders. Lancet 2012;380:689-98.
3. Steen VD, Medsger TA. Changes in causes of death in systemic sclerosis, 1972-2002. Annals of the rheumatic diseases 2007;66:940-4.
4. Tyndall AJ, Bannert B, Vonk M, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Annals of the rheumatic diseases 2010;69:1809-15.
5. Suliman YA, Dobrota R, Huscher D, et al. Brief Report: Pulmonary Function Tests: High Rate of False-Negative Results in the Early Detection and Screening of Scleroderma-Related Interstitial Lung Disease. Arthritis & rheumatology 2015;67:3256-61.
6. Steen VD, Conte C, Owens GR, Medsger TA, Jr. Severe restrictive lung disease in systemic sclerosis. Arthritis and rheumatism 1994;37:1283-9.
7. EndNote [software]. https://endnote.com
8. DistillerSR. Ottawa, Canada: Evidence Partners; 2013. http://systematic-review.net/
9. Wells GA, Shea B, O'Connell D, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2010. Available: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
10. Review Manager [software]. https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman
11. GRADEprofiler [software]. https://gradepro.org/

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

Project Plan – August 2022

ARDs included in this project

1. **Systemic sclerosis**
2. **Rheumatoid arthritis**
3. **Inflammatory myopathy**
4. **Sjogren's Syndrome**
5. **Mixed connective tissue disease**

SUMMARY OF PICO QUESTIONS

Screening PICO questions:

In people with ARD at increased risk of developing ILD, what is the impact of each of the following tests on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

- PFTs vs. history/physical
- High resolution CT thorax vs. history/physical
- 6-minute walk test distance vs. history/physical
- Chest radiograph vs. history/physical
- Ambulatory desaturation vs. history/physical
- Chest radiograph vs. high resolution CT thorax
- PFTs vs. ambulatory desaturation
- High resolution CT thorax vs. PFTs
- High resolution CT thorax and PFTs vs. PFTs alone
- Bronchoscopy vs. no bronchoscopy
- Surgical lung biopsy vs. no surgical lung biopsy

Monitoring PICO questions:

In people with ARD who also have ILD, what is the impact of each of the following tests on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

- PFTs vs. history/physical
- High resolution CT thorax vs. history/physical
- 6-minute walk test distance vs. history/physical
- Chest radiograph vs. history/physical
- Ambulatory desaturation vs. history/physical
- Chest radiograph vs. high resolution CT thorax
- Bronchoscopy vs. no bronchoscopy

- High resolution CT thorax vs. bronchoscopy
- PFTs vs. 6-minute walk test distance
- PFTs and 6-minute walk test distance vs. PFTs alone
- PFTs vs. ambulatory desaturation
- PFTs and high resolution CT thorax vs. PFTs alone
- 6-minute walk test distance vs. ambulatory desaturation

Medical management – 1st ILD therapy PICO questions:

In people with ARD who also have ILD, what is the impact of each of the following therapies as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

- Mycophenolate vs. no mycophenolate
- Cyclophosphamide vs. no cyclophosphamide (I/V or oral)
- Leflunomide vs. no leflunomide
- Methotrexate vs. no methotrexate
- Azathioprine vs. no azathioprine
- Calcineurin inhibitors vs. no calcineurin inhibitors
- Anti-TNF therapy vs. no anti-TNF therapy
- Abatacept vs. no abatacept
- Anti-CD20 antibody vs. no anti-CD20 antibody
- IL-6 receptor antagonists vs. no IL-6 receptor antagonists
- JAK inhibitors vs. no JAK inhibitors
- Daily oral prednisone vs. no daily oral prednisone
- IV pulse glucocorticoids vs. no IV pulse glucocorticoids
- Nintedanib vs. no nintedanib
- Pirfenidone vs. no pirfenidone
- IVIG vs. no IVIG
- Plasma exchange vs. no plasma exchange
- Adding nintedanib to mycophenolate vs. not adding nintedanib to mycophenolate
- Adding pirfenidone to mycophenolate vs. not adding pirfenidone to mycophenolate
- Upfront combination of nintedanib with mycophenolate vs. mycophenolate alone
- Upfront combination of pirfenidone with mycophenolate vs. mycophenolate alone
- Methotrexate vs. mycophenolate
- Leflunomide vs. mycophenolate
- Azathioprine vs. mycophenolate
- I/V or oral cyclophosphamide vs. mycophenolate
- Calcineurin inhibitors vs. mycophenolate

- TNF inhibitors vs. mycophenolate
- IL-6 receptor antagonists vs. mycophenolate
- Anti-CD20 antibody vs. mycophenolate
- Abatacept vs. mycophenolate
- JAK inhibitors vs. mycophenolate
- Nintedanib vs. mycophenolate
- Pirfenidone vs. mycophenolate
- IVIG vs. mycophenolate
- Oral prednisone vs. mycophenolate
- Intravenous methylprednisolone vs. mycophenolate
- Plasma exchange vs. mycophenolate
- Methotrexate vs. anti-CD20 antibody
- Leflunomide vs. anti-CD20 antibody
- Azathioprine vs. anti-CD20 antibody
- I/V or oral cyclophosphamide vs. anti-CD20 antibody
- Calcineurin inhibitors vs. anti-CD20 antibody
- TNF inhibitors vs. anti-CD20 antibody
- IL-6 receptor antagonists vs. anti-CD20 antibody
- Abatacept vs. anti-CD20 antibody
- JAK inhibitors vs. anti-CD20 antibody
- Nintedinib vs. anti-CD20 antibody
- Pirfenidone vs. anti-CD20 antibody
- IVIG vs. anti-CD20 antibody
- Oral prednisone vs. anti-CD20 antibody
- Intravenous methylprednisolone vs. anti-CD20 antibody
- Plasma exchange vs. anti-CD20 antibody
- Methotrexate vs. azathioprine
- Leflunomide vs. azathioprine
- I/V or oral cyclophosphamide vs. azathioprine
- Calcineurin inhibitors vs. azathioprine
- TNF inhibitors vs. azathioprine
- IL-6 receptor antagonists vs. azathioprine
  Abatacept vs. azathioprine
- JAK inhibitors vs. azathioprine
- Nintedinib vs. azathioprine

- Pirfenidone vs. azathioprine
- IVIG vs. azathioprine
- Oral prednisone vs. azathioprine
- Intravenous methylprednisolone vs. azathioprine
- Plasma exchange vs. azathioprine
- Methotrexate vs. I/V or oral cyclophosphamide
- Leflunomide vs. I/V or oral cyclophosphamide
- Calcineurin inhibitors vs. I/V or oral cyclophosphamide
- TNF inhibitors vs. I/V or oral cyclophosphamide
- IL-6 receptor antagonists vs. I/V or oral cyclophosphamide
- Abatacept vs. I/V or oral cyclophosphamide
- JAK inhibitors vs. I/V or oral cyclophosphamide
- Nintedinib vs. I/V or oral cyclophosphamide
- Pirfenidone vs. I/V or oral cyclophosphamide
- IVIG vs. I/V or oral cyclophosphamide
- Oral prednisone vs. I/V or oral cyclophosphamide
- Intravenous methylprednisolone vs. I/V or oral cyclophosphamide
- Plasma exchange vs. I/V or oral cyclophosphamide
- Nintedanib vs. IL-6 receptor antagonists
- Referral for stem cell transplant vs. optimal medical management
- Referral for lung transplant vs. optimal medical management

Medical management – ILD progression on any 1st ILD therapy PICO questions

In ARD patients with ILD progression after 1st ILD therapy, what is the impact of adding each of the following therapies on disease-related outcomes and treatment-related adverse events?

- Combination of nintedanib and mycophenolate vs. mycophenolate alone
- Combination of pirfenidone and mycophenolate vs. mycophenolate alone
- Methotrexate vs. mycophenolate
- Leflunomide vs. mycophenolate
- Azathioprine vs. mycophenolate
- I/V or oral cyclophosphamide vs. mycophenolate
- Calcineurin inhibitors vs. mycophenolate
- TNF inhibitors vs. mycophenolate
- IL-6 receptor antagonists vs. mycophenolate
- Anti-CD20 antibody vs. mycophenolate
- Abatacept vs. mycophenolate

- JAK inhibitors vs. mycophenolate
- Nintedinib vs. mycophenolate
- Pirfenidone vs. mycophenolate
- IVIG vs. mycophenolate
- Oral prednisone vs. mycophenolate
- Intravenous methylprednisolone vs. mycophenolate
- Plasma exchange vs. mycophenolate
- Methotrexate vs. anti-CD20 antibody
- Leflunomide vs. anti-CD20 antibody
- Azathioprine vs. anti-CD20 antibody
- I/V or oral cyclophosphamide vs. anti-CD20 antibody
- Calcineurin inhibitors vs. anti-CD20 antibody
- TNF inhibitors vs. anti-CD20 antibody
- IL-6 receptor antagonists vs. anti-CD20 antibody
- Abatacept vs. anti-CD20 antibody
- JAK inhibitors vs. anti-CD20 antibody
- Nintedinib vs. anti-CD20 antibody
- Pirfenidone vs. anti-CD20 antibody
- IVIG vs. anti-CD20 antibody
- Oral prednisone vs. anti-CD20 antibody
- Intravenous methylprednisolone vs. anti-CD20 antibody
- Plasma exchange vs. anti-CD20 antibody
- Methotrexate vs. azathioprine
- Leflunomide vs. azathioprine
- I/V or oral cyclophosphamide vs. azathioprine
- Calcineurin inhibitors vs. azathioprine
- TNF inhibitors vs. azathioprine
- IL-6 receptor antagonists vs. azathioprine
- Abatacept vs. azathioprine
- JAK inhibitors vs. azathioprine
- Nintedinib vs. azathioprine
- Pirfenidone vs. azathioprine
- IVIG vs. azathioprine
- Oral prednisone vs. azathioprine
- Intravenous methylprednisolone vs. azathioprine

- Plasma exchange vs. azathioprine
- Methotrexate vs. I/V or oral cyclophosphamide
- Leflunomide vs. I/V or oral cyclophosphamide
- Calcineurin inhibitors vs. I/V or oral cyclophosphamide
- TNF inhibitors vs. I/V or oral cyclophosphamide
- IL-6 receptor antagonists vs. I/V or oral cyclophosphamide
- Abatacept vs. I/V or oral cyclophosphamide
- JAK inhibitors vs. I/V or oral cyclophosphamide
- Nintedinib vs. I/V or oral cyclophosphamide
- Pirfenidone vs. I/V or oral cyclophosphamide
- IVIG vs. I/V or oral cyclophosphamide
- Oral prednisone vs. I/V or oral cyclophosphamide
- Intravenous methylprednisolone vs. I/V or oral cyclophosphamide
- Plasma exchange vs. I/V or oral cyclophosphamide
- Referral for stem cell transplant vs. optimal medical management
- Referral for lung transplant vs. optimal medical management

Medical management – rapidly progressive ILD PICO questions

In ARD patients with rapidly progressive ILD, what is the impact of each of the following therapies as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

- Daily oral prednisone vs. no daily oral prednisone
- Pulse intravenous glucocorticoids vs. no pulse intravenous glucocorticoids
- Nintedanib vs. no nintedanib
- Pirfenidone vs. no pirfenidone
- Adding nintedanib to mycophenolate vs. not adding nintedanib to mycophenolate
- Adding pirfenidone to mycophenolate vs. not adding pirfenidone to mycophenolate
- Upfront combination of nintedanib with mycophenolate vs. mycophenolate alone
- Upfront combination of pirfenidone with mycophenolate vs. mycophenolate alone
- Methotrexate vs. mycophenolate
- Leflunomide vs. mycophenolate
- Azathioprine vs. mycophenolate
- I/V or oral cyclophosphamide vs. mycophenolate
- Calcineurin inhibitors vs. mycophenolate
- TNF inhibitors vs. mycophenolate
- IL-6 receptor antagonists vs. mycophenolate
- Anti-CD20 antibody vs. mycophenolate

- Abatacept vs. mycophenolate
- JAK inhibitors vs. mycophenolate
- Nintedinib vs. mycophenolate
- Pirfenidone vs. mycophenolate
- IVIG vs. mycophenolate
- Oral prednisone vs. mycophenolate
- Intravenous methylprednisolone vs. mycophenolate
- Plasma exchange vs. mycophenolate
- Methotrexate vs. anti-CD20 antibody
- Leflunomide vs. anti-CD20 antibody
- Azathioprine vs. anti-CD20 antibody
- I/V or oral cyclophosphamide vs. anti-CD20 antibody
- Calcineurin inhibitors vs. anti-CD20 antibody
- TNF inhibitors vs. anti-CD20 antibody
- IL-6 receptor antagonists vs. anti-CD20 antibody
- Abatacept vs. anti-CD20 antibody
- JAK inhibitors vs. anti-CD20 antibody
- Nintedinib vs. anti-CD20 antibody
- Pirfenidone vs. anti-CD20 antibody
- IVIG vs. anti-CD20 antibody
- Oral prednisone vs. anti-CD20 antibody
- Intravenous methylprednisolone vs. anti-CD20 antibody
- Plasma exchange vs. anti-CD20 antibody
- Methotrexate vs. azathioprine
- Leflunomide vs. azathioprine
- I/V or oral cyclophosphamide vs. azathioprine
- Calcineurin inhibitors vs. azathioprine
- TNF inhibitors vs. azathioprine
- IL-6 receptor antagonists vs. azathioprine
- Abatacept vs. azathioprine
- JAK inhibitors vs. azathioprine
- Nintedinib vs. azathioprine
- Pirfenidone vs. azathioprine
- IVIG vs. azathioprine
- Oral prednisone vs. azathioprine

- Intravenous methylprednisolone vs. azathioprine
- Plasma exchange vs. azathioprine
- Methotrexate vs. cyclophosphamide
- Leflunomide vs. cyclophosphamide
- Calcineurin inhibitors vs. I/V or oral cyclophosphamide
- TNF inhibitors vs. I/V or oral cyclophosphamide
- of IL-6 receptor antagonists vs. I/V or oral cyclophosphamide
- Abatacept vs. I/V or oral cyclophosphamide
- JAK inhibitors vs. I/V or oral cyclophosphamide
- Nintedinib vs. I/V or oral cyclophosphamide
- Pirfenidone vs. I/V or oral cyclophosphamide
- IVIG vs. I/V or oral cyclophosphamide
- Oral prednisone vs. I/V or oral cyclophosphamide
- Intravenous methylprednisolone vs. I/V or oral cyclophosphamide
- Plasma exchange vs. I/V or oral cyclophosphamide
- Dual combination therapy* vs. monotherapy†
- Triple combination therapy‡ vs. monotherapy†
- Triple combination therapy‡ vs. dual combination therapy*
- IVIG and/or plasma exchange in addition to monotherapy†, dual combination therapy*, or triple combination therapy‡ vs. monotherapy†, dual combination therapy*, or triple combination therapy‡ alone
- Antifibrotic (e.g., nintedanib or pirfenidone) in addition to monotherapy†, dual combination therapy*, or triple combination therapy‡ vs. monotherapy†, dual combination therapy*, or triple combination therapy‡ alone
- Referral for stem cell transplant vs. optimal medical management
- Referral for lung transplant vs. optimal medical management

APPENDIX A – PICO Questions

Screening for ILD in people with rheumatic disease at increased risk of developing ILD

1. In people with rheumatic disease at increased risk of developing ILD, what is the impact of pulmonary function tests (PFTs) compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

2. In people with rheumatic disease at increased risk of developing ILD, what is the impact of high resolution CT thorax compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

3. In people with rheumatic disease at increased risk of developing ILD, what is the impact of 6-minute walk test distance compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

4. In people with rheumatic disease at increased risk of developing ILD, what is the impact chest radiograph compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

5. In people with rheumatic disease at increased risk of developing ILD, what is the impact of ambulatory desaturation compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

6. In people with rheumatic disease at increased risk of developing ILD, what is the impact of chest radiograph compared to high resolution CT thorax on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

7. In people with rheumatic disease at increased risk of developing ILD, what is the impact of pulmonary function tests (PFTs) compared to ambulatory desaturation on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

8. In people with rheumatic disease at increased risk of developing ILD, what is the impact of high resolution CT thorax compared to PFTs on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

9. In people with rheumatic disease at increased risk of developing ILD, what is the impact of high resolution CT thorax and PFTs compared to PFTs alone on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

10. In people with rheumatic disease at increased risk of developing ILD, what is the impact of bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy) compared to no bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy) on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

11. In people with rheumatic disease at increased risk of developing ILD, what is the impact of surgical lung biopsy compared to no surgical lung biopsy on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

Monitoring disease progression and treatment complications

12. In people with rheumatic disease with ILD, what is the impact of pulmonary function tests (PFTs) compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

13. In people with rheumatic disease with ILD, what is the impact of high resolution CT thorax compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

14. In people with rheumatic disease with ILD, what is the impact of 6-minute walk test distance compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination: crackles on auscultation) on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

15. In people with rheumatic disease with ILD, what is the impact of chest radiograph compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physical examination:

crackles on auscultation) on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

16. In people with rheumatic disease with ILD, what is the impact ambulatory desaturation compared to history/physical alone (e.g., shortness of breath (dyspnea), functional class and physician examination: crackles on auscultation) on responsiveness/sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

17. In people with rheumatic disease with ILD, what is the impact of chest radiograph compared to high resolution CT thorax on diagnostic accuracy, disease-related outcomes, and diagnostic testing-related adverse events?

18. In people with rheumatic disease with ILD, what is the impact of bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy) compared to no bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy) on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

19. In people with rheumatic disease with ILD, what is the impact of high resolution CT thorax compared to bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy) on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

20. In people with rheumatic disease with ILD, what is the impact of PFTs compared to 6-minute walk test distance on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

21. In people with rheumatic disease with ILD, what is the impact of PFTs and 6-minute walk test distance compared to PFTs alone on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

22. In people with rheumatic disease with ILD, what is the impact of PFTs compared to ambulatory desaturation on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

23. In people with rheumatic disease with ILD, what is the impact of PFTs and high resolution CT thorax compared to PFTs alone on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

24. In people with rheumatic disease with ILD, what is the impact of 6-minute walk test distance compared to ambulatory desaturation on responsiveness/ sensitivity to change of the test, disease-related outcomes, treatment-related serious adverse events and testing-related adverse events?

Medical Management

Rheumatic disease 1st ILD therapy

25. In people with rheumatic disease with ILD, what is the impact of mycophenolate compared to no mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

26. In people with rheumatic disease with ILD, what is the impact of cyclophosphamide compared to no cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

27. In people with rheumatic disease with ILD, what is the impact of leflunomide compared to no leflunomide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

28. In people with rheumatic disease with ILD, what is the impact of methotrexate compared to no methotrexate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

29. In people with rheumatic disease with ILD, what is the impact of azathioprine compared to no azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

30. In people with rheumatic disease with ILD, what is the impact of calcineurin inhibitors compared to no calcineurin inhibitors as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

31. In people with rheumatic disease with ILD, what is the impact of anti-TNF therapy compared to no anti-TNF therapy as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

32. In people with rheumatic disease with ILD, what is the impact of abatacept compared to no abatacept as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

33. In people with rheumatic disease with ILD, what is the impact of anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) compared to no anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

34. In people with rheumatic disease with ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to no IL-6 receptor antagonists (tocilizumab, sarilumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

35. In people with rheumatic disease with ILD, what is the impact of JAK inhibitors compared to no JAK inhibitors as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

36. In people with rheumatic disease with ILD, what is the impact of daily oral prednisone compared to no daily oral prednisone as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

37. In people with rheumatic disease with ILD, what is the impact of IV pulse glucocorticoids compared to no IV pulse glucocorticoids first line ILD treatment on disease-related outcomes and treatment-related adverse events?

38. In people with rheumatic disease with ILD, what is the impact of nintedanib compared to no nintedanib as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

39. In people with rheumatic disease with ILD, what is the impact of pirfenidone compared to no pirfenidone as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

40. In people with rheumatic disease with ILD, what is the impact of IVIG compared to no IVIG as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

41. In people with rheumatic disease with ILD, what is the impact of plasma exchange compared to no plasma exchange as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

42. In people with rheumatic disease with ILD without ILD progression, what is the impact of adding nintedanib to mycophenolate compared to not adding nintedanib to mycophenolate on disease-related outcomes and treatment-related adverse events?

43. In people with rheumatic disease with ILD without ILD progression, what is the impact of adding pirfenidone to mycophenolate compared to not adding pirfenidone to mycophenolate on disease-related outcomes and treatment-related adverse events?

44. In people with rheumatic disease with ILD, what is the impact of upfront combination of nintedanib with mycophenolate compared to mycophenolate alone as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

45. In people with rheumatic disease with ILD, what is the impact of upfront combination of pirfenidone with mycophenolate compared to mycophenolate alone as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

46. In people with rheumatic disease with ILD, what is the impact of methotrexate compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

47. In people with rheumatic disease with ILD, what is the impact of leflunomide compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

48. In people with rheumatic disease with ILD, what is the impact of azathioprine compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

49. In people with rheumatic disease with ILD, what is the impact of cyclophosphamide compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse

events?

50. In people with rheumatic disease with ILD, what is the impact of calcineurin inhibitors compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

51. In people with rheumatic disease with ILD, what is the impact of TNF inhibitors compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

52. In people with rheumatic disease with ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

53. In people with rheumatic disease with ILD, what is the impact of anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

54. In people with rheumatic disease with ILD, what is the impact of abatacept compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

55. In people with rheumatic disease with ILD, what is the impact of JAK inhibitors compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

56. In people with rheumatic disease with ILD, what is the impact of nintedinib compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

57. In people with rheumatic disease with ILD, what is the impact of pirfenidone compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

58. In people with rheumatic disease with ILD, what is the impact of IVIG compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

59. In people with rheumatic disease with ILD, what is the impact of oral prednisone compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

60. In people with rheumatic disease with ILD, what is the impact of intravenous methylprednisolone compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

61. In people with rheumatic disease with ILD, what is the impact of plasma exchange compared to mycophenolate as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

62. In people with rheumatic disease with ILD, what is the impact of methotrexate compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

63. In people with rheumatic disease with ILD, what is the impact of leflunomide compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

64. In people with rheumatic disease with ILD, what is the impact of azathioprine compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

65. In people with rheumatic disease with ILD, what is the impact of cyclophosphamide compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

66. In people with rheumatic disease with ILD, what is the impact of calcineurin inhibitors compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

67. In people with rheumatic disease with ILD, what is the impact of TNF inhibitors compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

68. In people with rheumatic disease with ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

69. In people with rheumatic disease with ILD, what is the impact of abatacept compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

70. In people with rheumatic disease with ILD, what is the impact of JAK inhibitors compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

71. In people with rheumatic disease with ILD, what is the impact of nintedinib compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

72. In people with rheumatic disease with ILD, what is the impact of pirfenidone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

73. In people with rheumatic disease with ILD, what is the impact of IVIG compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

74. In people with rheumatic disease with ILD, what is the impact of oral prednisone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

75. In people with rheumatic disease with ILD, what is the impact of intravenous methylprednisolone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

76. In people with rheumatic disease with ILD, what is the impact of plasma exchange compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

77. In people with rheumatic disease with ILD, what is the impact of methotrexate compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

78. In people with rheumatic disease with ILD, what is the impact of leflunomide compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

79. In people with rheumatic disease with ILD, what is the impact of cyclophosphamide compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

80. In people with rheumatic disease with ILD, what is the impact of calcineurin inhibitors compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

81. In people with rheumatic disease with ILD, what is the impact of TNF inhibitors compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

82. In people with rheumatic disease with ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

83. In people with rheumatic disease with ILD, what is the impact of abatacept compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

84. In people with rheumatic disease with ILD, what is the impact of JAK inhibitors compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

85. In people with rheumatic disease with ILD, what is the impact of nintedinib compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

86. In people with rheumatic disease with ILD, what is the impact of pirfenidone compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

87. In people with rheumatic disease with ILD, what is the impact of IVIG compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

88. In people with rheumatic disease with ILD, what is the impact of oral prednisone compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

89. In people with rheumatic disease with ILD, what is the impact of intravenous methylprednisolone compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

90. In people with rheumatic disease with ILD, what is the impact of plasma exchange compared to azathioprine as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

91. In people with rheumatic disease with ILD, what is the impact of methotrexate compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

92. In people with rheumatic disease with ILD, what is the impact of leflunomide compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

93. In people with rheumatic disease with ILD, what is the impact of calcineurin inhibitors compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

94. In people with rheumatic disease with ILD, what is the impact of TNF inhibitors compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

95. In people with rheumatic disease with ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

96. In people with rheumatic disease with ILD, what is the impact of abatacept compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related

adverse events?

97. In people with rheumatic disease with ILD, what is the impact of JAK inhibitors compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

98. In people with rheumatic disease with ILD, what is the impact of nintedinib compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

99. In people with rheumatic disease with ILD, what is the impact of pirfenidone compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

100. In people with rheumatic disease with ILD, what is the impact of IVIG compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

101. In people with rheumatic disease with ILD, what is the impact of oral prednisone compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

102. In people with rheumatic disease with ILD, what is the impact of intravenous methylprednisolone compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

103. In people with rheumatic disease with ILD, what is the impact of plasma exchange compared to cyclophosphamide as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

104. In people with rheumatic disease with ILD, what is the impact of nintedanib compared to IL-6 receptor antagonists (tocilizumab, sarilumab) as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

105. In people with rheumatic disease with ILD, what is the impact of referral for stem cell transplant compared to optimal medical management as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

106. In people with rheumatic disease with ILD, what is the impact of referral for lung transplant compared to optimal medical management as first line ILD treatment on disease-related outcomes and treatment-related adverse events?

Rheumatic disease with ILD progression after any 1st ILD therapy

107. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding the combination of nintedanib and mycophenolate compared to adding mycophenolate alone on disease-related outcomes and treatment-related adverse events?

108. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding the combination of pirfenidone and mycophenolate compared to adding mycophenolate alone on disease-related outcomes and treatment-related adverse events?

109. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding methotrexate compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

110. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding leflunomide compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

111. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding azathioprine compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

112. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding cyclophosphamide compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

113. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding calcineurin inhibitors compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

114. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding TNF inhibitors compared to adding mycophenolate on disease-related outcomes and treatment-

related adverse events?

115. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IL-6 receptor antagonists (tocilizumab, sarilumab) compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

116. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

117. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding abatacept compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

118. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding JAK inhibitors compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

119. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding nintedinib compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

120. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding pirfenidone compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

121. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IVIG compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

122. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding oral prednisone compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

123. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding intravenous methylprednisolone compared to adding mycophenolate on disease-related

outcomes and treatment-related adverse events?

124. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding plasma exchange compared to adding mycophenolate on disease-related outcomes and treatment-related adverse events?

125. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding methotrexate compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

126. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding leflunomide compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

127. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding azathioprine compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

128. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding cyclophosphamide compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

129. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding calcineurin inhibitors compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

130. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding TNF inhibitors compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

131. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IL-6 receptor antagonists (tocilizumab, sarilumab) compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

132. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding abatacept compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab,

ofatumumab) on disease-related outcomes and treatment-related adverse events?

133. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding JAK inhibitors compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

134. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding nintedinib compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

135. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding pirfenidone compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

136. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IVIG compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

137. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding oral prednisone compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

138. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding intravenous methylprednisolone compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

139. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding plasma exchange compared to adding anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) on disease-related outcomes and treatment-related adverse events?

140. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding methotrexate compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

141. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding leflunomide compared to adding azathioprine on disease-related outcomes and treatment-

related adverse events?

142. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding cyclophosphamide compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

143. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding calcineurin inhibitors compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

144. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding TNF inhibitors compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

145. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IL-6 receptor antagonists (tocilizumab, sarilumab) compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

146. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding abatacept compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

147. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding JAK inhibitors compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

148. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding nintedinib compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

149. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding pirfenidone compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

150. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IVIG compared to adding azathioprine on disease-related outcomes and treatment-related

adverse events?

151. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding oral prednisone compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

152. In people with rheumatic disease ILD progression after 1st ILD therapy, what is the impact of adding intravenous methylprednisolone compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

153. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding plasma exchange compared to adding azathioprine on disease-related outcomes and treatment-related adverse events?

154. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding methotrexate compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

155. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding leflunomide compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

156. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding calcineurin inhibitors compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

157. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding TNF inhibitors compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

158. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IL-6 receptor antagonists (tocilizumab, sarilumab) compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

159. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding abatacept compared to adding cyclophosphamide on disease-related outcomes and treatment-

related adverse events?

160. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding JAK inhibitors compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

161. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding nintedinib compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

162. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding pirfenidone compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

163. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding IVIG compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

164. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding oral prednisone compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

165. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding intravenous methylprednisolone compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

166. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of adding plasma exchange compared to adding cyclophosphamide on disease-related outcomes and treatment-related adverse events?

167. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of referral for stem cell transplant compared to optimal medical management on disease-related outcomes and treatment-related adverse events?

168. In people with rheumatic disease with ILD progression after 1st ILD therapy, what is the impact of referral for lung transplant compared to optimal medical management on disease-related outcomes and treatment-related adverse events?

Rheumatic disease with rapidly progressive ILD

169. In people with rheumatic disease with rapidly progressive ILD, what is the impact of daily oral prednisone compared to no daily oral prednisone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

170. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pulse intravenous glucocorticoids compared to no pulse intravenous glucocorticoids as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

171. In people with rheumatic disease with rapidly progressive ILD, what is the impact of nintedanib compared to no nintedanib as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

172. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pirfenidone compared to no pirfenidone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

173. In people with rheumatic disease with rapidly progressive ILD, what is the impact of adding nintedanib to mycophenolate compared to not adding nintedanib to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

174. In people with rheumatic disease with rapidly progressive ILD, what is the impact of adding pirfenidone to mycophenolate compared to not adding pirfenidone to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

175. In people with rheumatic disease with rapidly progressive ILD, what is the impact of upfront combination of nintedanib with mycophenolate compared to mycophenolate alone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

176. In people with rheumatic disease with rapidly progressive ILD, what is the impact of upfront combination of pirfenidone with mycophenolate compared to mycophenolate alone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

177. In people with rheumatic disease with rapidly progressive ILD, what is the impact of methotrexate compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes

and treatment-related adverse events?

178. In people with rheumatic disease with rapidly progressive ILD, what is the impact of leflunomide compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

179. In people with rheumatic disease with rapidly progressive ILD, what is the impact of azathioprine compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

180. In people with rheumatic disease with rapidly progressive ILD, what is the impact of cyclophosphamide compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

181. In people with rheumatic disease with rapidly progressive ILD, what is the impact of calcineurin inhibitors compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

182. In people with rheumatic disease with rapidly progressive ILD, what is the impact of TNF inhibitors compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

183. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

184. In people with rheumatic disease with rapidly progressive ILD, what is the impact of anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

185. In people with rheumatic disease with rapidly progressive ILD, what is the impact of abatacept compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

186. In people with rheumatic disease with rapidly progressive ILD, what is the impact of JAK inhibitors compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes

and treatment-related adverse events?

187. In people with rheumatic disease with rapidly progressive ILD, what is the impact of nintedinib compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

188. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pirfenidone compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

189. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IVIG compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

190. In people with rheumatic disease with rapidly progressive ILD, what is the impact of oral prednisone compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

191. In people with rheumatic disease with rapidly progressive ILD, what is the impact of intravenous methylprednisolone compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

192. In people with rheumatic disease with rapidly progressive ILD, what is the impact of plasma exchange compared to mycophenolate as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

193. In people with rheumatic disease with rapidly progressive ILD, what is the impact of methotrexate compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

194. In people with rheumatic disease with rapidly progressive ILD, what is the impact of leflunomide compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

195. In people with rheumatic disease with rapidly progressive ILD, what is the impact of azathioprine compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line

rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

196. In people with rheumatic disease with rapidly progressive ILD, what is the impact of cyclophosphamide compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

197. In people with rheumatic disease with rapidly progressive ILD, what is the impact of calcineurin inhibitors compared to anti-CD20 (rituximab, ocrelizumab, obinutuzumab, ofatumumab) antibody as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

198. In people with rheumatic disease with rapidly progressive ILD, what is the impact of TNF inhibitors compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

199. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

200. In people with rheumatic disease with rapidly progressive ILD, what is the impact of abatacept compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

201. In people with rheumatic disease with rapidly progressive ILD, what is the impact of JAK inhibitors compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

202. In people with rheumatic disease with rapidly progressive ILD, what is the impact of nintedinib compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

203. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pirfenidone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

204. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IVIG compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

205. In people with rheumatic disease with rapidly progressive ILD, what is the impact of oral prednisone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

206. In people with rheumatic disease with rapidly progressive ILD, what is the impact of intravenous methylprednisolone compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

207. In people with rheumatic disease with rapidly progressive ILD, what is the impact of plasma exchange compared to anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab) as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

208. In people with rheumatic disease with rapidly progressive ILD, what is the impact of methotrexate compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

209. In people with rheumatic disease with rapidly progressive ILD, what is the impact of leflunomide compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

210. In people with rheumatic disease with rapidly progressive ILD, what is the impact of cyclophosphamide compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

211. In people with rheumatic disease with rapidly progressive ILD, what is the impact of calcineurin inhibitors compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

212. In people with rheumatic disease with rapidly progressive ILD, what is the impact of TNF inhibitors compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

213. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

214. In people with rheumatic disease with rapidly progressive ILD, what is the impact of abatacept compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

215. In people with rheumatic disease with rapidly progressive ILD, what is the impact of JAK inhibitors compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

216. In people with rheumatic disease with rapidly progressive ILD, what is the impact of nintedinib compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

217. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pirfenidone compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

218. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IVIG compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

219. In people with rheumatic disease with rapidly progressive ILD, what is the impact of oral prednisone compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

220. In people with rheumatic disease with rapidly progressive ILD, what is the impact of intravenous methylprednisolone compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

221. In people with rheumatic disease with rapidly progressive ILD, what is the impact of plasma exchange compared to azathioprine as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

222. In people with rheumatic disease with rapidly progressive ILD, what is the impact of methotrexate compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

223. In people with rheumatic disease with rapidly progressive ILD, what is the impact of leflunomide compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

224. In people with rheumatic disease with rapidly progressive ILD, what is the impact of calcineurin inhibitors compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

225. In people with rheumatic disease with rapidly progressive ILD, what is the impact of TNF inhibitors compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

226. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IL-6 receptor antagonists (tocilizumab, sarilumab) compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

227. In people with rheumatic disease with rapidly progressive ILD, what is the impact of abatacept compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

228. In people with rheumatic disease with rapidly progressive ILD, what is the impact of JAK inhibitors compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

229. In people with rheumatic disease with rapidly progressive ILD, what is the impact of nintedinib compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

230. In people with rheumatic disease with rapidly progressive ILD, what is the impact of pirfenidone compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

231. In people with rheumatic disease with rapidly progressive ILD, what is the impact of IVIG compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

232. In people with rheumatic disease with rapidly progressive ILD, what is the impact of oral prednisone compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

233. In people with rheumatic disease with rapidly progressive ILD, what is the impact of intravenous methylprednisolone compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

234. In people with rheumatic disease with rapidly progressive ILD, what is the impact of plasma exchange compared to cyclophosphamide as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

235. In people with rheumatic disease with rapidly progressive ILD, what is the impact of dual combination therapy* compared to monotherapy† as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

236. In people with rheumatic disease with rapidly progressive ILD, what is the impact of triple combination therapy‡ compared to monotherapy† as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

237. In people with rheumatic disease with rapidly progressive ILD, what is the impact of triple combination therapy‡ compared to dual combination therapy* as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

238. In people with rheumatic disease with rapidly progressive ILD, what is the impact of using IVIG and/or plasma exchange in addition to monotherapy†, dual combination therapy*, or triple combination therapy‡ compared to using monotherapy†, dual combination therapy*, or triple combination therapy‡ alone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

239. In people with rheumatic disease with rapidly progressive ILD, what is the impact of using an antifibrotic (e.g., nintedanib or pirfenidone) in addition to monotherapy†, dual combination therapy*, or triple combination therapy‡ compared to using monotherapy†, dual combination therapy*, or triple

combination therapy‡ alone as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

240. In people with rheumatic disease with rapidly progressive ILD, what is the impact of referral for stem cell transplant compared to optimal medical management as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

241. In people with rheumatic disease with rapidly progressive ILD, what is the impact of referral for lung transplant compared to optimal medical management as first line rapidly progressive ILD treatment on disease-related outcomes and treatment-related adverse events?

† Monotherapy examples: oral prednisone/intravenous methylprednisolone, or mycophenolate, or azathioprine, or a calcineurin inhibitor, or rituximab, or cyclophosphamide

* Dual combination therapy examples: oral prednisone/intravenous methylprednisolone and mycophenolate, or oral prednisone/intravenous methylprednisolone and azathioprine, or oral prednisone/intravenous methylprednisolone and a calcineurin inhibitor, or oral prednisone/intravenous methylprednisolone and rituximab, or oral prednisone/intravenous methylprednisolone and cyclophosphamide, or oral prednisone/intravenous methylprednisolone and a JAK inhibitor

‡ Triple combination therapy examples: oral prednisone/intravenous methylprednisolone and rituximab and cyclophosphamide, or oral prednisone/intravenous methylprednisolone and cyclophosphamide and a calcineurin inhibitor, or oral prednisone/intravenous methylprednisolone and mycophenolate and a calcineurin inhibitor, or oral prednisone/intravenous methylprednisolone and mycophenolate and abatacept, or oral prednisone/intravenous methylprednisolone and rituximab and mycophenolate

APPENDIX B – INCLUSION/EXCLUSION CRITERIA

POPULATIONS

Include

- Adults
- Rheumatoid arthritis, Systemic sclerosis (Scleroderma), Mixed Connective Tissue Disease (MCTD), Polymyositis, Dermatomyositis, MDA5 Dermatomyositis, Immune Mediated Necrotizing Myositis, Antisynthetase syndrome, Sjogren's syndrome
- Progressive Fibrosing ILD

Exclude

- Pediatrics (age 16 or younger)
- Juvenile scleroderma, juvenile systemic sclerosis, juvenile dermatomyositis, juvenile idiopathic arthritis
- Sarcoidosis, Interstitial Pneumonia with Autoimmune Features (IPAF), ankylosing spondylitis, ANCA-associated vasculitis, Systemic lupus erythematosus, Undifferentiated connective tissue disease
- Idiopathic Pulmonary Fibrosis
- Idiopathic interstitial pneumonias
- Unclassifiable ILD
- Overlap syndromes (e.g., SSc+myositis, RA+SSc, et)

INTERVENTIONS

Include

- Pulmonary Function Tests (PFTs)
- History/physical alone (e.g., shortness of breath (dyspnea), functional class and physician examination: crackles on auscultation)
- High resolution CT Thorax
- 6-minute walk test distance
- Ambulatory desaturation
- Chest radiograph (chest x-ray)
- Bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy)
- Surgical lung biopsy
- csDMARDs: methotrexate, leflunomide, azathioprine, cyclophosphamide, mycophenolate, calcineurin inhibitors (tacrolimus, cyclosporine)
- bDMARDs: TNF inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), IL-6 receptor antagonists (tocilizumab, sarilumab), anti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab), abatacept

- tsDMARDs: JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
- Others: Oral prednisone, intravenous methylprednisolone, intravenous immunoglobulin (IVIG), plasma exchange (plasmapheresis)
- Antifibrotics: Pirfenidone, Nintedanib
- Stem cell transplant (autologous, mesenchymal stem cells, hematopoietic, myeloablative, non-myeloablative)
- Lung Transplant

Exclude

- Vaccines: influenza, COVID-19, MMR, pneumococcus vaccine (refer to 2022 ACR vaccine guideline, presently in journal review; summary is online)
- Education (self-management of oxygen, ILD disease) *(will mention in Introduction or Discussion section)*
- Physiotherapy (chest physiotherapy, airway clearance, incentive spirometry), Exercise (aerobic, resistance training, yoga, tai chi), Pulmonary Rehabilitation (cardio-pulmonary rehabilitation, resistance training, in a center versus home)
- Oxygen (oxygen desaturation at rest, oxygen desaturation <88% with exercise)
- Palliative care (cough, pain, air hunger, end stage, end of life planning, when to initiate, what to initiate)
- Smoking cessation
- Fundoplication
- GI medications: proton pump inhibitors, H2 blockers, promotility agents
- Ibritumomab (is anti-CD20, but it is radioimmunotherapy)
- Basiliximab

COMPARATORS

Include

- No test
- History/physical alone (e.g., shortness of breath (dyspnea), functional class and physician examination: crackles on auscultation)
- High resolution CT Thorax
- Bronchoscopy (may include broncho-alveolar lavage, transbronchial biopsy, cryobiopsy)
- 6-minute walk test distance
- Ambulatory desaturation
- PFTs
- Placebo, no treatment
- Mycophenolate
- antiAnti-CD20 antibody (rituximab, ocrelizumab, obinutuzumab, ofatumumab)
- Azathioprine
- Cyclophosphamide

- Stem cell transplant (autologous, mesenchymal stem cells, hematopoietic, myeloablative, non-myeloablative)
- Lung transplant

OUTCOMES *(see Appendix C)*

STUDY DESIGN (includes only studies published in English language)

For all PICO questions, we will include randomized or non-randomized controlled trials (this includes case-control studies). To capture adverse events, we will also consider open-label extension studies of RCTs or other longitudinal observational studies that focus on safety and tolerability. For PICO questions that focus on assessing the accuracy of screening tools, we will also include studies without an independent control group, specifically cohort and cross-sectional studies. We will also include existing systematic reviews and guidelines from other societies **only** to confirm that we have included all relevant reference.

Include

- RCTs, including:
  - Open-label extensions of RCTs with placebo involved
- Non-randomized controlled studies, including
  - Case-control studies
- Cohort studies
- Cross-sectional studies
- Longitudinal studies (focusing on safety and tolerability)
- Systematic reviews and Guidelines from other societies

[NOTE: If there has been a recently done, well-done systematic review on the exact PICO that ACR is asking, then that systematic review could be considered for use in the guideline; primary study data would still need to be pulled in the ACR's database, though.]

Exclude

- Abstracts
- Case reports
- Narrative reviews
- Prevalence studies
- Economic studies, e.g., cost-effectiveness studies
- Drug adherence studies
- Studies of risk factors
- Foreign language studies
- Studies with irrelevant population, interventions, or outcomes
- Animal studies

APPENDIX C: OUTCOMES

Screening

Critical outcomes:

- Diagnostic accuracy
- Disease-related outcomes[1]
- Diagnostic testing-related adverse events

Monitoring

Critical outcomes:

- Responsiveness/sensitivity to change of the test
- Disease-related outcomes[1]
- Treatment-related serious adverse events
- Testing-related adverse events

Medical management

- Disease-related outcomes[1]
- Treatment-related adverse events

[1]**Critical outcomes:** mortality, disability, health related quality of life, adverse events (serious adverse events, toxicity leading to discontinuation). **Surrogate outcomes:** disease activity/disease progression defined by forced vital capacity (FVC), diffusion capacity for carbon monoxide (DLCO), CT thorax: extent of disease, disease progression.

APPENDIX D: DISCLOSURES

Participant Disclosures - American College of Rheumatology (ACR) Guideline for the Screening, Monitoring, and Treatment of Interstitial Lung Disease in Patients with Systemic Autoimmune Rheumatic Disease

In order for the College to most effectively further its mission and to otherwise maintain its excellent reputation in the medical community and with the public, it is important that confidence in the College's integrity be maintained. The cornerstone of the ACR's Disclosure Policy is disclosure of actual and potential conflicts so that they can be evaluated by the College in order to avoid undue influence of potential conflicts. The purpose of the ACR's Disclosure Policy is identification of relationships which may pose actual or potential conflicts. These actual or potential conflicts can then be evaluated by the College so that adjustments can be made that will avoid any undue influence. This policy is based on the principle that, in many cases, full disclosure of the actual or potentially conflicting relationship will of itself suffice to protect the integrity of the College and its interests.

Participants	Role	Primary Employer	Interest Held By	Interest Type	Entity/Licensee	Additional Information	Value
Sindhu R. Johnson	Core Team - Co-PI	Toronto Western Hospital	Self	Independent Contractor - Editorial Board	Best Practice and Clinical Rheumatology		
			Self	Independent Contractor - Associate Editor	Journal of Rheumatology		
			Spouse/Partner	Independent Contractor - Editorial Board Member	Anesthesiology		
			Spouse/Partner	Independent Contractor - Editorial Board Member	Canadian Journal of Anesthesia		
			Spouse/Partner	Independent Contractor - Consultant	Edwards Lifesciences		
			Spouse/Partner	Independent Contractor - Consultant	Surgical Safety Technologies		
			Spouse/Partner	Independent Contractor - Editorial Board Member	Circulation Journal		
Elana Bernstein	Core Team - Co-PI	Columbia University/New York-Presbyterian Hospital	Self	Grant / Contract	U.S. Department of Defense		$750,000.00
			Self	Employment	James J. Peters VA Medical Center		
			Self	Employment	Columbia University		
			Self	Grant / Contract	Scleroderma Research Foundation	Columbia receives fees from the Scleroderma Research Foundation based on the number of new patient study visits and follow-up patient	$52,000.00

						study visits conducted.	
			Self	Grant / Contract	National Institutes of Health		$801,500.00
			Self	Independent Contractor - IC Iloprost for SSc-associated Raynaud's	Eicos	Total direct costs: $16,358.19 per patient	
			Self	Independent Contractor - Data And Safety Monitoring	UCLA Health System		$20,000.00
			Self	Independent Contractor - A Phase 2, Open-label, Multicenter Study to Evaluate the Efficacy and Safety of Belumosudil in dcSSc	Kadmon Pharmaceuticals LLC	Total direct costs: $40,697 per patient	
			Self	Grant / Contract	Boehringer Ingelheim		$500,000.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$6,526.25
			Self	Grant / Contract	Pfizer		$150,000.00
			Self	Independent Contractor - Scientific Advisory Board	Boehringer Ingelheim	I did not accept any compensation for participating in this Scientific Advisory Board.	

Marcy B. Bolster	Core Team - Content expert	Massachusetts General Hospital	Self	Grant / Contract	Genentech	Clinical trial I helped with data collection but did not receive salary support from this trial. I am not privy to the contracted amount. I thought I should disclose my relationship since my name is listed as a co-investigator and co-author on the publication. Please let me know if additional information is needed.	$1.00
			Self	Grant / Contract	Cumberland Pharmaceuticals	I am a co-investigator for this clinical trial	$31,699.00
			Self	Independent Contractor - Consultant	Merck Sharp & Dohme Corporation		
			Self	Independent Contractor - Associate Editor	PracticeUpdate		$10,000.00
			Self	Independent Contractor - Member, ABIM Rheumatology Longitudinal Assessment Program (LAP)Approval Committee	American Board of Internal Medicine		
			Self	Independent Contractor - Co-investigator	Corbus		
			custodial account with child who is no longer a dependent	Stock	Johnson and Johnson		$5,000.00
			Self	Independent Contractor - Principal Investigatory	Rheumatology Research Foundation	Grant recipient for salary support	
			Self	Independent Contractor - Principal Investigatory	Rheumatology Research Foundation	Grant recipient for salary support	

Jonathan H. Chung	Core Team - Content expert	University of Chicago				Nothing to disclose	
Sonye Danoff	Core Team - Content expert	Johns Hopkins University School of Medicine	Self	Grant / Contract	Boehringer Ingelheim	Open label extension of INBUILD clinical trial	$15,000.00
			Self	Grant / Contract	Boehringer Ingelheim		$500,000.00
			Self	Independent Contractor - Consultant	CSL Behring	This is a 4- hour virtual multi-disciplinary advisory board on autoimmune myositis	$3,000.00
			Self	Grant / Contract	Bristol Myers Squibb Company	This is a clinical trial of an LPA inhibitor in Progressive-fibrosing ILD	$125,000.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$2,600.00
			Self	Independent Contractor - Data And Safety Monitoring	Galapagos		$1,000.00
			Self	Employment	Pulmonary Fibrosis Foundation		
			Self	Fiduciary Officer	American Thoracic Society		
Michael George	Core Team - Content expert	Penn Medicine	Self	Independent Contractor - Consultant	AbbVie		$4,085.00
			Self	Employment	Perelman School of Medicine, University of Pennsylvania		
			Self	Independent Contractor - Consultant	Global Healthy Living Foundation		
			Self	Grant / Contract	GlaxoSmithKline		$61,000.00
			Self	Independent Contractor - Consultant	Dysimmune Diseases Foundation		$2,600.00
			Self	Independent Contractor - Consultant	Global Healthy Living Foundation		$3,000.00
Dinesh Khanna	Core Team - Content expert	University of Michigan	Self	Independent Contractor - Consultant	Genentech Foundation		$4,000.00
			Self	Independent Contractor - Consultant	CSL Behring		$1,000.00
			Self	Independent Contractor - Consultant	AbbVie		$4,000.00
			Self	Independent Contractor - Consultant	Actelion Pharmaceuticals		$6,000.00
			Self	Independent Contractor - Consultant	Prometheus		$5,000.00

			Self	Independent Contractor - Consultant	Horizon Pharma plc		$20,000.00
			Self	Stock Option	Eicos Sciences	Chief Medical Officer	
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$80,000.00
Ilya Ivlev	Core Team - Literature Review Co-Leader	ECRI Institute	Self	Grant / Contract	U.S. Department of Defense	Role-co-lead	$0.00
			Self	Grant / Contract	Agency for Healthcare Research and Quality	Goal 1: The purpose of this Task Order is to conduct systematic evidence reviews that the Task Force will use to make new or update existing recommendations Goal 2: To synthesize available evidence to support primary care guidelines development.	$0.00
			Self	Independent Contractor - Affiliate Investigator	Kaiser Permanente		
			Self	Grant / Contract	National Institute on Aging		$60,000.00
			Self	Employment	ECRI		
			Self	Grant / Contract	National Cancer Institute	To synthesize available evidence to support primary care guidelines development. Role: Research Curator, evidence synthesis for actionability	$0.00
			Self	Employment	Kaiser Permanente		
			Self	Grant / Contract	Agency for Healthcare Research and Quality		$300,000.00

Stacey Uhl	Core Team - Literature Review Co-Leader	ECRI Institute				Nothing to disclose	
Gordon Guyatt	Core Team - GRADE Expert	McMaster University				Nothing to disclose	
Reza Mirza	Core Team - GRADE/Methodological Contributor	McMaster University				Nothing to disclose	
Sandeep Agarwal	Lit Review Team	Baylor College of Medicine				Nothing to disclose	
Danielle Antin-Ozerkis	Lit Review Team	Yale School of Medicine	Self	Grant / Contract	Pliant Therapeutics	Grant paid to institution for work completed, patients enrolled	$130,999.00
			Self	Grant / Contract	Galacto Biotech AB	Grant paid to institution for work completed, patients enrolled	$116,975.00
			Self	Grant / Contract	Galapagos	Grant paid to institution for work completed, patients enrolled	$181,000.00
			Self	Grant / Contract	FibroGen	Grant paid to institution for work completed, patients enrolled	$133,000.00
			Self	Stock	Amgen		$100,000.00
			Self	Grant / Contract	Boehringer Ingelheim	Grant paid to institution for work completed, patients enrolled	$126,683.00
			Self	Grant / Contract	Boehringer Ingelheim	Grant paid to institution for work completed, patients enrolled	$120,811.00
			Self	Stock	Pfizer		$15,000.00
			Self	Stock	AbbVie		$100,000.00

			Self	Grant / Contract	Genentech	Grant paid to institution for work completed, patients enrolled	$211,000.00
Bradford Bemiss	Lit Review Team	Loyola University Medical Center	Self	Independent Contractor - Speakers bureau	Boehringer Ingelheim		
Vaidehi Chowdhary	Lit Review Team	Yale School of Medicine	Self	Independent Contractor - International Editor	International Journal of Rheumatic Diseases		
			Self	Grant / Contract	MCIC vermont	Title: Communication and Management of Test Results in Patients Initiating Biologic Agents PI on the Grant awarded to the section. No compensation for salary, or consultation. No effort paid for self.	$75,000.00
			Self	Independent Contractor - International editorial board member	Indian Journal of Rheumatology		
Jane E. Dematte D'Amico	Lit Review Team	Northwestern Medicine	Self	Independent Contractor - Site Principal Investigator	United Therapeutics Corporation		
			Self	Independent Contractor - Site Principle Investigator	FibroGen		
			Self	Independent Contractor - Site Prinicipal Investigator	Genentech		
			Self	Independent Contractor - Site Principal Investigator	Boehringer Ingelheim		
Robert Hallowell	Lit Review Team	Massachusetts General Hospital	Self	Independent Contractor - Consultant	Genentech		$4,000.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$2,500.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$5,000.00
			Self	Medical Advisory board for the Myositis Association.			

Alicia M. Hinze	Lit Review Team	Mayo Clinic	Contract with my Employer Mayo Clinic	Grant / Contract	Rheumatology Research Foundation	Career development award which supports engagement in research and career development activities to evaluate radiomic biomarkers for ILD progression in systemic sclerosis.	$375,000.00
			Self	Grant / Contract	Mayo Clinic	Career Development Award supporting 0.1FTE and some research expenses	$150,000.00
			Self	Employment	Mayo Clinic	Division of Rheumatology, full time, hybrid research and clinical position	
Patil A. Injean	Lit Review Team	Cedars-Sinai				Nothing to disclose	
Nikhil Jiwrajka	Lit Review Team	Penn Medicine	Self	Grant / Contract	Perelman School of Medicine, University of Pennsylvania		$15,000.00
			Self	Employment	Perelman School of Medicine, University of Pennsylvania		
			Self	Grant / Contract	Perelman School of Medicine, University of Pennsylvania		$40,000.00
Elena Joerns	Lit Review Team	UT Southwestern Medical Center	Self	Employment	University of Texas Southwestern Medical Center		
			Self	Grant / Contract	Pfizer Inc.	22.7% effort	$50,000.00

			T32 training grant supporting Elena Joerns' salary	Grant / Contract	National Institute of Health	The major goals of this project are to perform a detailed phenotypic analysis of immunosuppressed patients with interstitial pneumonia with autoimmune features in the UTSW cohort and assess predictors of response to immunosuppression.	$259,496.00
Joyce Lee	Lit Review Team	University of Colorado	Self	Independent Contractor - Consultant	Boehringer Ingelheim		$1,200.00
			Self	Grant / Contract	Boehringer Ingelheim	Only start up costs have been received, the milestone based payment of the remainder of the grant has been delayed due to the pandemic.	$500,000.00
			Self	Grant / Contract	Boehringer Ingelheim	Aryeh Fischer was site PI originally, transferred to me beginning August 2019 after his departure	$128,954.00
			Self	Grant / Contract	Bristol-Myers Squibb		$18,320.00
			Self	Grant / Contract	Boehringer Ingelheim	my role is co-investigator	$491,453.00
			Self	Grant / Contract	Novartis		$71,253.00
			Self	Independent Contractor - Consultant	Pulmonary Fibrosis Foundation	They support 25% of my time	

			Self	Grant / Contract	FibroGen		$30,455.00
			Self	Grant / Contract	U.S. Department of Defense	my role is co-investigator	$9,969,396.00
			Self	Employment	Pulmonary Fibrosis Foundation	They support 25% of my time	
			Self	Grant / Contract	National Heart, Lung, and Blood Institute		$576,298.00
			Self	Independent Contractor - Consultant	ElevenP15		$6,000.00
			Self	Independent Contractor - Data And Safety Monitoring	United Therapeutics Corporation		$1,000.00
			Self	Independent Contractor - Data And Safety Monitoring	SyneosHealth		$2,000.00
			Self	Independent Contractor - Member of the ILD editorial board	Chest Journal		
			Self	Employment	university of Colorado school of medicine		
			Self	Grant / Contract	UCLA Health System	Aryeh Fischer was site PI originally, transferred to me beginning August 2019 after his departure	$93,553.00
			Self	Grant / Contract	National Heart, Lung, and Blood Institute	My role is co-investigator	$6,195,411.00
			Self	Independent Contractor - Co-chair of program committee	American Thoracic Society		
			Self	Grant / Contract	Galapagos	close out ongoing	$33,291.00
			Self	Independent Contractor - Consultant	United Therapeutics Corporation		$800.00

Ashima Makol	Lit Review Team	Mayo Clinic	Self	Independent Contractor - Co-investigator for clinical trial sub study	Boehringer Ingelheim	No compensation. Nailfold capillaroscopy substudy complete more than 2 years ago. SENSCIS-ON participants are seen periodically for physical exams.	
			Self	Employment	Mayo Clinic		
			Self	Independent Contractor - Site PI for the KD025-209 study	Kadmon Corporation LLC	No personal compensation. Costs are study execution costs on site. Trial recently closed to recruitment by Sanofi. No further recruitment activity at our site.	$22,630.00
			Self	Independent Contractor - Medical content contributor	Figure1		$1,300.00
			Self	Independent Contractor - HZN-825 in Patients With Diffuse Cutaneous Systemic Sclerosis	Horizon Therapeutics plc	Phase Study is not active yet but plan to activate april/may 2022 at our site.	
Gregory McDermott	Lit Review Team	Massachusetts General Hospital	Self	Employment	Partners Healthcare		
			Self	Employment	Brigham and Women's Hospital	Clinical Fellow	
Jake G Natalini	Lit Review Team	NYU Langone Health				Nothing to disclose	
Justin Oldham	Lit Review Team	University of California, Davis	Self	Independent Contractor - Consultant	Boehringer Ingelheim		$20,000.00
			Self	Independent Contractor - Consultant	United Therapeutics Corporation		$3,000.00
			Self	Independent Contractor - Consultant	F. Hoffmann-La Roche		$5,800.00
			Self	Independent Contractor - Consultant	Lupin Pharmaceuticals, Inc		$5,000.00
Didem Saygin	Lit Review Team	University of Chicago				Nothing to disclose	

Kimberly Showalter Lakin	Lit Review Team	Hospital for Special Surgery, Weill Cornell Medicine				Nothing to disclose	
Namrata Singh	Lit Review Team	University of Washington	Self	Grant / Contract	American Heart Association		$200,000.00
			Self	Grant / Contract	Rheumatology Research Foundation		$375,000.00
Joshua J. Solomon	Lit Review Team	National Jewish Health	Self	Independent Contractor - Investigator Initiated Grant Funding	Boehringer Ingelheim	30,000 total grant funding for 2022	$30,000.00
			Self	Independent Contractor - CTD ILD education	Boehringer Ingelheim		$6,000.00
			Self	Independent Contractor - PI TRAIL1 Trial	Genentech		$14,000.00
			Self	Grant / Contract	PFIZER CANADA INC		$82,904.00
Jeffrey Sparks	Lit Review Team	Brigham and Women's Hospital	Self	Independent Contractor - Consultant	Amgen		
			Self	Independent Contractor - Consultant	Bristol-Myers Squibb		
			Self	Independent Contractor - Consultant	AbbVie		
Marat Turgunbaev	Lit Review Team	American College of Rheumatology				Nothing to disclose	
Samera Vaseer	Lit Review Team	University of Oklahoma				Nothing to disclose	
Rohit Aggarwal	Voting Panel	University of Pittsburgh Medical Center	Self	Independent Contractor - Consultant	Scipher		
			Self	Intellectual Property - Other Intellectual Property		Under University of Pittsburgh	
			Self	Independent Contractor - Consultant	Kezar		
			Self	Independent Contractor - Consultant	Alexion Pharmaceuticals, Inc.		
			Self	Independent Contractor - Consultant	E.R. Squibb & Sons, L.L.C.		
			Self	Grant / Contract	E.R. Squibb & Sons, L.L.C.		$148,531.84
			Self	Independent Contractor - Consultant	Galapagos		
			Self	Independent Contractor - Consultant	Mallinckrodt LLC		
			Self	Independent Contractor - Consultant	argenx		
			Self	Independent Contractor - Consultant	EMD Serono		
			Self	Independent Contractor - Consultant	corbus		
			Self	Independent Contractor - Consultant	kyverna		
			Self	Independent Contractor - Consultant	Horizon Therapeutics plc		

			Self	Independent Contractor - Consultant	Merck		
			Self	Grant / Contract	Mallinckrodt Hospital Products Inc.		
			Self	Grant / Contract	Q32		$10,000.00
			Self	Independent Contractor - Consultant	AstraZeneca Pharmaceuticals LP		
			Self	Independent Contractor - Consultant	Roivant		
			Self	Grant / Contract	Mallinckrodt LLC		$75,000.00
			Self	Grant / Contract	EMD Serono		$10,000.00
			Self	Independent Contractor - Consultant	Q32		
			Self	Independent Contractor - Consultant	Janssen Global Services, LLC		
			Self	Independent Contractor - Consultant	CSL Behring		
			Self	Independent Contractor - Consultant	Janssen Biotech, Inc.		
			Self	Independent Contractor - Consultant	AbbVie Inc.		
			Self	Independent Contractor - Consultant	Teva Pharmaceutical Industries		
			Self	Independent Contractor - Consultant	Boehringer Ingelheim Pharmaceuticals, Inc.		
			Self	Independent Contractor - Consultant	Octapharma USA, Inc.		
			Self	Independent Contractor - Consultant	Pfizer		
Shervin Assassi	Voting Panel	Texas Health Science Center Houston	Self	Grant / Contract	National Institute of Health		$783,582.00
			Self	Independent Contractor - Section Editor	Current Opinions in Rheumatology		
			Self	Grant / Contract	Scleroderma Research Foundation		$467,797.00
			Self	Independent Contractor - Editorial Board	Arthritis Research and Therapy		
			Self	Grant / Contract	National Institute of Health		$1,710,960.00
			Self	Independent Contractor - Speaker bureau	Integrity continuous education		$2,500.00
			Self	Employment	The University of Texas Health Science Center at Houston		
			Self	Grant / Contract	National Institute of Health		$346,497.00
			Self	Independent Contractor - Consultant	AstraZeneca		$4,296.00
			Self	Independent Contractor - Speaker	North Carolina Rheumatology Association		$4,000.00

			Self	Independent Contractor - President	scleroderma clinical trial consortium	This is a non-profit, global organization for improving quality of clinical research in systemic sclerosis.	
			Self	Independent Contractor - Consultant	Boehringer Ingelheim	I have not yet received any compensation yet but the estimated compensation for 2022 is $15,000 to $20,000.	
			Self	Grant / Contract	Boehringer Ingelheim		$127,084.00
			Self	Grant / Contract	Boehringer Ingelheim		$108,383.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$21,465.59
			Self	Independent Contractor - Consultant	CSL Behring		$2,115.00
			Self	Grant / Contract	Janssen Biotech, Inc.		$246,254.00
			Self	Independent Contractor - Consultant	AbbVie		$2,250.00
Lenore Buckley	Voting Panel	Yale School of Medicine				Nothing to disclose	
Paul F. Dellaripa	Voting Panel	Brigham and Women's Hospital	Self	Independent Contractor - committee member	Food and Drug Administration		
			Self	Independent Contractor - Clincal investigator	Genentech		
			Self	Independent Contractor - Clincal investigator	Bristol-Myers Squibb	no payment of money to me	
			Self	Independent Contractor - committee member	Boehringer Ingelheim		
Robyn T. Domsic	Voting Panel	University of Pittaburgh Medical Center	Self	Independent Contractor - Consultant	CSL Behring		
Tracy Doyle	Voting Panel	Brigham and Women's Hospital	Self	Grant / Contract	Genentech	Site PI for TRAIL1 clinical trial (0.12 calendar months or 1% effort). $9,750 total cost, $7,500 direct cost per year.	$9,750.00

Tracy M. Frech	Voting Panel	Vanderbilt University Medical Center				Nothing to disclose	
Monique E. Hinchcliff	Voting Panel	Yale School of Medicine	Self	Grant / Contract	Boehringer Ingelheim		$950,231.00
Cheilonda Johnson	Voting Panel	Penn Medicine				Nothing to disclose	
Jeffrey P. Kanne	Voting Panel	University of Wisconsin School of Medicine and Public Health	Self	Independent Contractor - Consultant	Calyx.ai	Independent reviewer for clinical trials - 1 hour per week	$15,000.00
			Self	Independent Contractor - Consultant	Bayer Healthcare	Intermittent clinical trial work	$5,000.00
			Self	Independent Contractor - Consultant	Elsevier		$1,000.00
			Self	Independent Contractor - Consultant	Delfi Diagnostics	$350 per hour up to 20 hours	$475.00
			Self	Independent Contractor - Consultant	Wolters Klewer Health, Inc.		$3,000.00
John S. Kim	Voting Panel	University of Virginia School of Medicine	Self	Grant / Contract	Pulmonary Fibrosis Foundation		$50,000.00
			Self	Grant / Contract	National Heart, Lung, and Blood Institute		$171,612.00
Scott Matson	Voting Panel	University of Kansas Medical Center	Self	Employment	School of Medicine, University of Kansas		
			Self	Independent Contractor - Consultant	imvaria diagnostics		
Zsuzsanna McMahan	Voting Panel	Johns Hopkins University School of Medicine	Self	Grant / Contract	Jerome L. Greene Foundation		$50,000.00
			Self	Grant / Contract	National Institute of Health		$149,703.00
			Self	Grant / Contract	Corbus Pharmaceuticals Holdings	I was a sub-PI who did skin biopsies; I did get salary support for each biopsy I perform (~1% total)	$1,200.00
			Self	Independent Contractor - ACR Representative to the Ex Officio Advisory Board	World Scleroderma Foundation		
			Self	Intellectual Property - Other Intellectual Property			

Lee Shapiro	Voting Panel	Albany Medical College				Nothing to disclose	
Christine D. Sharkey	Voting Panel	University of Wisconsin School of Medicine and Public Health				Nothing to disclose	
Ross S. Summer	Voting Panel	Thomas Jefferson University Hospital	Self	Independent Contractor - Horizon Trial IPF	Horizon Pharma plc		
John Varga	Voting Panel	University of Michigan	Self	Independent Contractor - Consultant	Emerald pharma		
			Self	Independent Contractor - Consultant	up to date		
			Self	Independent Contractor - editor	current rheumatology reports		
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		$4,000.00
			Self	Independent Contractor - Consultant	Best doctors		
			Self	Independent Contractor - EIC	WILEY		$5,000.00
			Self	Independent Contractor - Consultant	Boehringer Ingelheim		
			Self	Independent Contractor - Consultant	TeneoBio Pharma		$20,000.00