American College Of Rheumatology
Updated Guideline for the Management of Rheumatoid Arthritis

Project Plan – October 2018

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ORGANIZATIONAL LEADERSHIP AND SUPPORT

This updated clinical practice guideline is being developed by the American College of Rheumatology (ACR) with funding by the ACR.

BACKGROUND

Rheumatoid arthritis (RA) is an autoimmune disease, the most common type of inflammatory arthritis that affects more than 1.3 million Americans. Of these, about 75% are women. The disease most often begins between the fourth and sixth decades of life; however, RA can start at any age. Symptoms commonly include joint tenderness, joint swelling and pain. Blood test results for RA patients typically show the presence of rheumatoid factor, antibodies to cyclic citrullinated peptides (anti-CCP), and an elevated erythrocyte sedimentation rate or C-reactive protein.

Although the cause of RA is not known, research is providing more knowledge about what makes the immune system attack the body and create inflammation in the joints, and what role genetics plays. Evidence suggests that activation of immune cells leads to an imbalance between pro-inflammatory and anti-inflammatory cytokines. The hallmarks of RA are synovitis (affecting joints and periarticular structures including tendon sheaths), extra-articular features such as nodules, interstitial lung disease, vasculitis, etc., and systemic inflammation that can lead to early and/or accelerated atherosclerosis and premature heart disease and stroke.

The goals of RA treatment are to improve patients' quality of life by reducing symptoms, reducing functional limitations, preventing joint damage, and decreasing complications of the disease.

The mainstays of treatment have been conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate and sulfasalazine. An array of targeted biologic therapies have now been approved to treat RA. In addition, new targeted oral small molecule agents have become available. With the availability of more treatment options and more information about existing therapies, updated recommendations are needed to help clinicians optimize the care of patients with RA.

OBJECTIVES

The objective of this project is to develop recommendations for the medical management of patients with RA. Specifically, we aim to:

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1. Develop recommendations for the use of disease-modifying anti-rheumatic drugs (DMARDs) (including conventional synthetic DMARDs, targeted biologic DMARDs and targeted synthetic DMARDs), as well as glucocorticoids.
2. Clarify differences in treatment recommendations for patients who are DMARD-naïve versus those who have already been treated with one or more DMARDs.
3. Clarify differences in treatment recommendations for patients with low versus moderate to high disease activity.
4. Develop recommendations for tapering DMARDs.
5. Include recommendations for non-pharmacologic therapies in the management of RA.
6. Include recommendations related to co-morbid conditions (e.g., congestive heart failure, hepatitis B or C, cancer, history of serious infections).
7. Include recommendations for vaccine administration.

Note, recommendations related to reproductive health are covered in a separate guideline (expected release date early 2019). Recommendations regarding the impact of imaging on treatment decisions will be addressed in future updates. Readers will be referred to the 2015 ACR RA guidelines for recommendations related to screening and monitoring.

METHODS

Identification of Studies

Literature search strategies, based on PICO questions (Population/patients, Intervention, Comparator, and Outcomes; *see Appendix A*) will be developed by the principal investigators, systematic literature review leader, and a research librarian, with input from the Core Team. The search strategies will be peer reviewed by another medical librarian using Peer Review of Electronic Search Strategies (PRESS) (1). Searches will be performed in OVID Medline (1946 +), Embase (1974 +), the Cochrane Library, and PubMed (mid-1960s +).

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

Search Limits

Only English language articles will be retrieved.

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Grey Literature

The websites of appropriate agencies, such as the Agency for Healthcare Research and Quality (AHRQ), will be searched for peer-reviewed reports not indexed by electronic databases.

Literature Search Update

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

Inclusion/Exclusion Criteria

See PICO questions (*Appendix A*), which outline the defined patient population, interventions, comparators and outcomes.

Management of Studies and Data

References and abstracts will be imported into bibliographic management software (Reference Manager) (2), duplicates removed, and exported to Distiller SR, a web-based systematic review manager (3). Screening 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 about interventions aimed at the pharmacologic and non-pharmacologic management of RA will be performed to determine existing studies covering outcomes of interest. Subsequently, identified studies will be assessed using the RevMan (4) and GRADE Pro tools (5).
2. Chosen studies will be assessed for risk of bias using modified versions of the Cochrane Risk of Bias tool (6) and the Newcastle-Ottawa Scale (7).
3. Additionally, recently published systematic reviews covering outcomes of interest will also be sought and used for reference cross-checking.

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GRADE Methodology

GRADE methodology (8) 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 strength of recommendations will be graded as strong or conditional. 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.

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) (4) and GRADEprofiler (GRADEpro) software (5). 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 eight rheumatologists, one occupational therapist, one physician assistant, and two patient representatives, 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 the voting panel meeting agenda. At the face-to-face voting panel meeting, chaired by the principal investigator, 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 literature review leader, the GRADE expert, and

selected members of the literature review team, who will attend the meeting to provide details about the evidence, as requested. Voting panel discussions and decisions will 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. GRADE evidence profiles and summary of findings tables for each PICO question

AUTHORSHIP

Authorship of the guideline will include: principal investigator, Dr. Liana Fraenkel, as the lead author and voting panel leader; Dr. Elie A. Akl, literature review leader and GRADE expert; Drs. Joan M. Bathon, Bryant England, and E. William St. Clair, content experts. Members of the literature review team and voting panel will also be authors. The PI 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 B for participant disclosures.*

REFERENCES

1. Sampson M, McGowan J, Lefebvre C, Moher D, Grimshaw J. PRESS: Peer Review of Electronic Search Strategies. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2008.
2. Reference Manager [software]. Thomson Reuters; 2013. http://www.refman.com/
3. DistillerSR. Ottawa, Canada: Evidence Partners; 2013. http://systematic-review.net/
4. Review Manager [software]. Oxford (UK): Cochrane Collaboration; 2013. http://ims.cochrane.org/revman
5. GRADEprofiler [software]. Oxford (UK): Cochrane Collaboration; 2013. http://ims.cochrane.org/revman/gradepro

6. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available: http://handbook.cochrane.org.
7. 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
8. GRADE guidelines - best practices using the GRADE framework. 2013. Available: http://www.gradeworkinggroup.org/publications/JCE2011.htm

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APPENDIX A – PICO Questions

DMARD = Refers to any csDMARD, boDMARD or tsDMARD

DMARD Groups

csDMARDs	boDMARDs	tsDMARDs
Methotrexate (MTX)	TNF Inhibitors	JAK Inhibitors
Hydroxychloroquine (HCQ)	• Etanercept	• Tofacitinib
Sulfasalazine (SSZ)	• Adalimumab	• Baricitinib
Leflunomide (LEF)	• Certolizumab	
	• Golimumab	
	• Infliximab	
	Abatacept	
	Rituximab	
	IL-6 Receptor Inhibitors	
	• Tocilizumab	
	• Sarilumab	

GC = glucocorticoids / steroids (prednisone, or equivalent); PROM = patient reported outcome measure

INITIAL THERAPY

1. Should patients with DMARD-naïve RA and low disease activity receive MTX monotherapy or an alternative csDMARD monotherapy?
P - Patients with DMARD-naïve RA and low disease activity
I - MTX monotherapy
C - HCQ
C - SSZ
C - LEF
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

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2. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX monotherapy or an alternative csDMARD monotherapy?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - MTX monotherapy
C - HCQ
C - SSZ
C - LEF
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

3. Should patients with DMARD-naïve RA and low disease activity receive csDMARD monotherapy or csDMARD combination (double or triple) therapy?
P - Patients with DMARD-naïve RA and low disease activity
I - csDMARD monotherapy
C - csDMARD double combination therapy
C - csDMARD triple combination therapy
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

4. Should patients with DMARD-naïve RA and moderate to high disease activity receive csDMARD monotherapy or combination (double or triple) therapy?
P - Patients with DMARD-naïve RA who have moderate to high disease activity
I - csDMARD monotherapy
C - csDMARD double combination therapy
C - csDMARD triple combination therapy
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

5. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX monotherapy or boDMARD monotherapy or tsDMARD monotherapy?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - MTX monotherapy
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor

O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

6. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX monotherapy or boDMARD with MTX or tsDMARD with MTX?
P -Patients with DMARD-naïve RA and moderate to high disease activity
I - MTX monotherapy
C - TNF Inhibitor + MTX
C - Abatacept+ MTX
C - Rituximab+ MTX
C - IL-6 Receptor Inhibitor+ MTX
C - JAK Inhibitor + MTX
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for subpopulations with varying risk factors.

7. Should patients with DMARD-naïve RA and moderate to high disease activity receive mono- or combination csDMARDs and *short-term (< 3 months)* GCs or mono or combination csDMARDs alone?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - Mono or combination csDMARDs with short-term (< 3 months) GCs
C - Mono or combination csDMARDs alone (i.e., without short-term GCs)
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes
Recommendations may differ for different doses of GCs.

8. Should patients with DMARD-naïve RA and moderate to high disease activity, receive *long-term (≥ 3 months)* low dose (≤ 10mg per day) GCs and mono- or combination csDMARDs or mono or combination csDMARDs alone?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - Mono or combination csDMARDs with long-term (≥ 3 months) low dose (≤ 10mg per day) GCs
C - Mono or combination csDMARDs alone (i.e. without long-term GCs)
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

INITIAL ADMINISTRATION OF MTX

9. Should patients with RA initiating MTX receive oral MTX or subcutaneous (SC) MTX?
P - Patients with RA initiating MTX
I - Oral MTX
C - SC MTX

O - Disease activity, PROMs, treatment-related harms, treatment persistence

10. Should patients with RA initiating MTX receive MTX at 15mg or more per week (includes up-titrating to 15mg over the first month) or less than 15mg per week as the initial dose?
P - Patients with RA initiating MTX
I - MTX < 15mg per week
C - MTX 15mg per week
C - MTX 20 mg per week
C - MTX 25mg per week
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

11. Should patients with RA initiating oral MTX receive MTX as a single or split dose (over < 24 hours)?
P - Patients with RA initiating oral MTX
I - MTX single dose
C - MTX split dose
O - Disease activity, PROMs, treatment-related harms, treatment persistence

Treat-to-Target (T2T)

12. Should patients with RA receive T2T strategies or usual care?
P - Patients with RA
I - T2T strategy
C - Usual care
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

13. In patients with RA receiving T2T, should the treatment goal be low disease activity or remission?
P - Patients with RA
I - Treat to low disease activity
C - Treat to remission
O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

14. In patients with RA receiving T2T who are NOT at target, should the interval for treatment escalation be 3 months versus less than 3 months after the last DMARD change?
P - Patients with RA receiving T2T, who have recently added or switched DMARD(s) and are not at target
I - Escalate treatment 3 months or later after the last DMARD change
C - Escalate treatment less than 3 months after the last DMARD change
O - Disease activity, PROMs, treatment-related harms, long-term outcomes

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TREATMENT ESCALATION

15. Should patients with RA not tolerating MTX, on folic acid 1 mg/day, increase the dose of folic acid?
P - Patients with RA not tolerating MTX on 1mg of folic acid
I - Increase dose of folic acid to > 1mg per day
C - Remain on folic acid 1 mg per day
O - Disease activity, PROMs, treatment-related harms, treatment persistence

16. Should patients with RA not tolerating oral MTX receive a split dose (over < 24 hours) or subcutaneous (SC) MTX?
P - Patients with RA not tolerating oral MTX
I - Split oral MTX
C - SC MTX
O - Disease activity, PROMs, treatment-related harms, treatment persistence

17. Should patients with RA not tolerating MTX, switch to alternative mono or combination csDMARDs, to a boDMARD, or to a tsDMARD?
P - Patients with RA not tolerating MTX monotherapy (either oral or SC)
I - Switch to non-MTX mono or combination csDMARDs
C - Switch to TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence, long-term outcomes

18. Should patients with RA on oral MTX monotherapy 15 mg per week who are NOT at target increase the dose of oral MTX or switch to SC MTX?
P - Patients with RA on oral MTX monotherapy 15 mg per week who are not at target
I - Increase the dose of oral MTX
C - Switch to SC MTX
O - Disease activity, PROMs, treatment-related harms, treatment persistence

19. Should patients with RA on maximally tolerated dose of MTX monotherapy who are NOT at target add SSZ and HCQ, add LEF, add a boDMARD, or add a tsDMARD?

P - Patients with RA on maximally tolerated dose of MTX monotherapy (either oral or SC) who are not at target
I - Add SSZ and HCQ
C - Add LEF
C - Add TNF Inhibitor
C - Add Abatacept
C - Add Rituximab
C - Add IL-6 Receptor Inhibitor
C - Add JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence, long-term outcomes

20. Should patients with RA on maximally tolerated dose of LEF monotherapy who are NOT at target, and have previously failed MTX (due to an inadequate response or adverse events), add SSZ and HCQ, or add a boDMARD, or add tsDMARD?
P - Patients with RA on maximally tolerated dose of LEF monotherapy who are not at target, and have previously failed MTX (due to an inadequate response or adverse events)
I - Add SSZ and HCQ
C - Add TNF Inhibitor
C - Add Abatacept
C - Add Rituximab
C - Add IL-6 Receptor Inhibitor
C - Add JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, long-term outcomes

21. Should patients with RA on DMARD(s) who are not on GCs and are NOT at target switch to another DMARD, add a 2nd DMARD, switch to another DMARD and add GCs *short-term (< 3 months),* or add both a 2nd DMARD and GCs *short-term (< 3 months)*?
P - Patients with RA on DMARD(s) not on GCs who are not at target
I - Switch to another DMARD
C - Add another DMARD
C - Switch to another DMARD and add short-term (< 3 months) GCs
C - Add another DMARD and add short short-term (< 3 months) GCs
O - Disease activity, PROMs, treatment-related harms, treatment persistence
Recommendations may differ for different doses of GCs and for different classes of DMARDs.

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22. Should patients with RA on DMARD(s) not on GCs and NOT at target switch DMARDs, add a 2nd DMARD, switch DMARDs and add GCs *long-term (≥ 3 months),* or add both a 2nd DMARD and GCs *long-term (≥ 3 months)*?
P - Patients with RA on DMARD(s) not on GCs who are not at target
I - Switch to another DMARD
C - Add another DMARD
C - Switch to another DMARD and add long-term (≥ 3 months) GCs
C - Add another DMARD and add short long-term (≥ 3 months) GCs
O - Disease activity, PROMs, treatment-related harms, treatment persistence
Recommendations may differ for different doses of GCs and for different classes of DMARDs.

23. Should patients with RA on DMARD(s) requiring GCs to remain at target, add a 2nd DMARD or switch to another DMARD to enable tapering off of GCs?
P - Patients with RA on DMARD(s) requiring GCs to remain at target
I - No change to management
C - Switch to another DMARD
C - Add a 2nd DMARD
O - Disease activity, PROMs, treatment-related harms, long-term outcomes
Recommendations may differ for different doses of GCs and for different classes of DMARDs.

24. Should patients with RA on their first TNF Inhibitor who are NOT at target, switch to a 2nd TNF Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?
P - Patients with RA on their first TNF Inhibitor who are not at target
I - Switch to a 2nd TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

25. Should patients with RA on their 2nd TNF Inhibitor who are NOT at target, switch to a 3rd TNF Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?
P - Patients with RA on their 2nd TNF Inhibitor who are not at target
I - Switching to a 3rd TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor

C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

26. Should patients with RA on their first IL-6 Receptor Inhibitor who are NOT at target, switch to a 2nd IL-6 Receptor Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?
P - Patients with RA on their first IL-6 Receptor Inhibitor who are not at target
I - Switch to a 2nd IL-6 Receptor Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to TNF Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

27. Should patients with RA on their first JAK Inhibitor who are NOT at target, switch to a 2nd JAK Inhibitor or switch to a boDMARD?
P - Patients with RA on their first JAK Inhibitor who are not at target
I - Switch to a 2nd JAK Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to TNF Inhibitor
C - Switch to IL-6 Receptor Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

INTRAARTICULAR (IA) Corticosteroids

28. Should patients with RA on DMARDs and synovitis in 1 or 2 joints who are NOT at target receive IA corticosteroids alone or add/switch DMARDs or IA corticosteroids and add/switch DMARD(s)?
P - Patients with RA on DMARDs with synovitis in 1 or 2 joints who are not at target
I - IA steroids
C - Add DMARD(s)
C - Switch DMARD(s)
C - IA steroids and add DMARD(s)
C - IA steroids and switch DMARD(s)
O - Disease activity, PROMs, treatment-related harms, treatment persistence

Recommendations may differ for different classes of DMARDs.

NON-PHARMACOLOGIC THERAPY vs. DMARDs

29. Should patients with DMARD-naïve RA and low disease activity use any specific diet or DMARDs?
P - Patients with DMARD-naïve RA and low disease activity
I - Specific diet
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

30. Should patients with DMARD-naïve RA and moderate to high disease activity use any specific diet or DMARDs?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - Specific diet
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

31. Should patients with DMARD-naïve RA and low disease activity use any specific nutraceutical or DMARDs?
P - Patients with DMARD-naïve RA and low disease activity
I - Specific nutraceutical
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

32. Should patients with DMARD-naïve RA and moderate to high disease activity use any specific nutraceutical or DMARDs?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - Specific nutraceutical
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

33. Should patients with DMARD-naïve RA and low disease activity do any specific exercise or take DMARDs?
P - Patients with DMARD-naïve RA and low disease activity
I - Specific exercise
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

34. Should patients with DMARD-naïve RA and moderate to high disease activity do any specific exercise or take DMARDs?
P - Patients with DMARD-naïve RA and moderate to high disease activity
I - Specific exercise
C - DMARDs
O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

NON-PHARMACOLOGIC THERAPY IN ADDITION TO DMARDs

35. Should patients with RA on DMARDs use a specific diet?
P - Patients with RA on DMARDs
I - Specific diet
C - No specific diet
O - Disease activity, PROMs (*pain and fatigue), treatment-related harms, long term outcomes

36. Should patients with RA on DMARDs use a specific nutraceutical?
P - Patients with RA on DMARDs
I - Specific nutraceuticals
C - No specific nutraceuticals
O - Disease activity, PROMs, treatment-related harms, long term outcomes

37. Should patients with RA on DMARDs use a standardized self-management program?
P - Patients with RA on DMARDs
I - Standardized self-management program
C - No standardized self-management program
O - Disease activity, PROMs (*pain and fatigue), arthritis self-efficacy, treatment-related harms, long term outcomes

38. Should patients with RA on DMARDs do aerobic exercise?
P - Patients with RA on DMARDs
I - Aerobic exercise
C - No aerobic exercise
O - Disease activity, PROMs (*pain and fatigue), treatment-related harms, long term outcomes

39. Should patients with RA on DMARDs do aquatic exercise?
P - Patients with RA on DMARDs

I - Aquatic exercise
C - No aquatic exercise
O - Disease activity, PROMs (*pain and fatigue), treatment-related harms, long term outcomes

40. Should patients with RA on DMARDs do resistance and strengthening exercises?
P - Patients with RA on DMARDs
I - Resistance and strengthening exercises
C - No resistance or strengthening exercises
O - Disease activity, PROMs (*pain and fatigue), treatment-related harms, long term outcomes

41. Should patients with RA and hand/wrist involvement on DMARDs use splinting/orthoses?
P - Patients with RA and hand/wrist involvement on DMARDs
I - Wrist splinting/orthoses
C - No splinting/orthoses
O - Disease activity, PROMs (*pain and function), objective measures of hand function, treatment-related harms, long term outcomes

42. Should patients with RA and foot/ankle involvement on DMARDs use orthoses?
P - Patients with RA on DMARDs and foot involvement
I - Orthoses
C - No orthoses
O - Disease activity, PROMs (*pain and function), treatment-related harms, long term outcomes

43. Should patients with RA and hand involvement on DMARDs do hand exercises?
P - Patients with RA and hand involvement on DMARDs
I - Hand exercises
C - No hand exercises
O - Disease activity, PROMs (*pain and function), objective measures of hand function, treatment-related harms, long term outcomes

44. Should patients with RA on DMARDs use joint protection techniques?
P - Patients with RA on DMARDs
I - Joint protection
C - No joint protection
O - Disease activity, PROMs (*pain and function), objective measures of function, treatment-related harms, long term outcomes

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45. Should patients with RA on DMARDs use mind-body approaches?
P - Patients with RA on DMARDs
I - Mind-body approaches
C - No mind-body approaches
O - Disease activity, PROMs (*pain), arthritis self-efficacy, treatment-related harms, long term outcomes

46. Should patients with RA on DMARDs, who are currently employed or want to become employed, use work interventions?
P - Patients with RA on DMARDs, who are currently employed or want to become employed
I - Work interventions
C - No work interventions
O - Work-related outcomes

47. Should patients with RA on DMARDs participate in occupational therapy?
P - Patients with RA on DMARDs
I - Comprehensive occupational therapy
C - No comprehensive occupational therapy
O - Disease activity, PROMs (*pain and function), arthritis self-efficacy, objective measure of function, treatment-related harms, long term outcomes

48. Should patients with RA on DMARDs participate in physical therapy?
P - Patients with RA on DMARDs
I - Comprehensive physical therapy
C - No comprehensive physical therapy
O - Disease activity, PROMs (*pain and function), arthritis self-efficacy, objective measure of function, treatment-related harms, long term outcomes

49. Should patients with RA on DMARDs who are overweight or obese lose weight?
P - Patients with RA on DMARDs who are overweight or obese
I - Weight loss
C - No weight loss
O - Disease activity, PROMs (*pain, fatigue, function, QOL), long term outcomes

50. Should patients with RA on DMARDs who are current smokers stop smoking?
P - Patients with RA on DMARDs
I - Stop smoking
C - Continue smoking

O - Disease activity, PROMs (*pain), long term outcomes

51. Should patients with RA on DMARDs use acupuncture?
P - Patients with RA on DMARDs
I - Acupuncture
C - No acupuncture
O - Disease activity, PROMs (*pain), treatment-related harms, long term outcomes

TAPERING OFF (i.e., gradual lowering dose with intent to discontinue)

52. Should patients with RA on DMARDs who are <u>in low disease activity</u> taper off DMARDs or not taper off DMARDS?
P - Patients with RA on DMARDs who are in low disease activity
I - Taper off DMARDs
C - Continue DMARDs at same dose
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

53. Should patients with RA on DMARDs who are <u>in remission</u> taper off DMARDs or not taper off DMARDS?
P - Patients with RA on DMARDs in remission
I - Taper off
C - Continue DMARDs at same dose
O - Disease activity, PROMs, treatment-related harms, time to flare, regain remission

54. Should patients with RA on DMARDs who are at target taper off DMARDs after 6 months of being at target or after longer than 6 months of being at target?
P - Patients with RA on DMARDs at target
I - Taper off DMARDs after 6 months of being at target
C - Taper off DMARDs after longer than 6 months of being at target
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

55. Should patients with RA on DMARDs and low dose GCs (≤ 10mg per day) who are at target taper off or continue low dose GCs?
P - Patients with RA on DMARDs and low dose GCs (≤ 10mg per day) who are at target
I - Taper off low dose GCs
C - Continue low dose GCs
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

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654
655
656
657 ***TAPERING PATIENTS ON MONOTHERAPY***
658
659 **56. Should patients with RA on DMARD monotherapy who are in remission taper off the DMARD or**
660 **continue the DMARD at the same dose?**
661 P - Patients with RA on DMARD monotherapy who are in remission
662 I - Taper off DMARD
663 C - Continue DMARD at same dose
664 O - Disease activity, PROMs, treatment-related harms, time to flare, regain remission
665 ***Recommendations may differ for subpopulations with varying risk factors.***
666
667 **57. Should patients with RA on DMARD monotherapy who are in low dose activity taper off or**
668 **continue the DMARD?**
669 P - Patients with RA on DMARD monotherapy who are in low dose activity
670 I - Taper off DMARD
671 C - Continue DMARD at same dose
672 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target
673 ***Recommendations may differ for subpopulations with varying risk factors.***
674
675 ***TAPERING OFF PATIENTS ON MORE THAN 1 DMARD***
676
677 **58. Should patients with RA on triple therapy (MTX + SSZ + HCQ) who are at target taper off MTX or**
678 **taper off alternative csDMARDs?**
679 P - Patients with RA on triple therapy who are at target
680 I - Taper off MTX
681 C - Taper off alternative csDMARDs
682 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target
683
684 **59. Should patients with RA on MTX + boDMARD or MTX + tsDMARD who are at target taper off MTX**
685 **or taper off the boDMARD or the tsDMARD?**
686 P - Patients with RA on MTX + boDMARD or MTX + tsDMARD who are at target
687 I - Taper off MTX
688 C - Taper off the boDMARD or the tsDMARD
689 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target
690

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LOWERING DMARD DOSE (Decrease dose or increase interval and maintain at lower dose)

60. Should patients with RA on DMARD monotherapy who are at target lower the dose or increase the interval between doses or continue the DMARD at the same dose?
P - Patients with RA on DMARD monotherapy in remission
I - Continue DMARD at the same dose
C - Lower the dose of the DMARD
C - Increase the interval between DMARD doses
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target
Recommendations may differ for different classes of DMARDs.

61. Should patients with RA on MTX + boDMARD or tsDMARD who are at target continue MTX at the same dose or lower the dose of MTX? (boDMARD or tsDMARD continued at same dose)
P - Patients with RA on MTX + boDMARD or tsDMARD who are at target
I - Continue MTX at the same dose
C - Lower the dose of MTX
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

62. Should patients with RA on MTX + boDMARD or tsDMARD who are at target continue the boDMARD or tsDMARD at the same dose or lower the dose or increase the interval between doses of the boDMARD or tsDMARD (MTX continued at same dose)?
P - Patients with RA on MTX + boDMARD or tsDMARD who are at target
I - Continue the same dose of the boDMARD or tsDMARD
C - Lower the dose of the boDMARD or tsDMARD
C - Increase the interval between the doses of the boDMARD or tsDMARD
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

63. Should patients with RA on MTX + boDMARD or tsDMARD who are at target lower the dose of MTX or lower the dose or increase the interval between doses of the boDMARD or tsDMARD?
P - Patients with RA on MTX + boDMARD or tsDMARD who are at target
I - Lower the dose of MTX
C - Lower the dose of the boDMARD or tsDMARD
C - Increase the interval between doses of boDMARD or tsDMARD
O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

ADVERSE EVENT ISSUES

64. Should patients with RA with (progressive) subcutaneous nodules, who are NOT at target and are not on MTX, start MTX or alternative DMARDs?
P - Patients with RA and (progressive) subcutaneous nodules, who are not at target, are not on MTX
I - Start MTX
C - Start alternative csDMARD mono or combination therapy
C - Start TNF Inhibitor
C - Start Abatacept
C - Start Rituximab
C - Start IL-6 Receptor Inhibitor
C - Start JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, nodule progression

65. Should patients with RA with (progressive) subcutaneous nodules, who are at target and are on MTX, continue MTX or switch to alternative DMARD(s)?
P - Patients with RA and (progressive) subcutaneous nodules who are at target and are on MTX
I - Continue MTX
C - Switch to alternative csDMARD mono or combination therapy
C - Switch to TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, nodule progression

66. Should patients with RA who have persistent hypogammaglobulinemia after RTX treatment continue RTX or switch to csDMARD mono or combination therapy or to a boDMARD targeting a different molecule or to a tsDMARD?
P - Patients with RA who have persistent hypogammaglobulinemia after RTX treatment
I - Continue RTX
C - Switch to csDMARD mono or combination therapy
C - Switch to TNF Inhibitor
C - Switch to Abatacept
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms

PARENCHYMAL LUNG DISEASE

67. Should patients with DMARD-naïve RA who have clinical parenchymal lung disease receive MTX or alternative DMARD(s) for treatment of joint disease?

P - Patients with DMARD-naïve RA and parenchymal lung disease
I - Start MTX
C - Start alternative csDMARD mono or combination therapy
C - Start TNF Inhibitor
C - Start Abatacept
C - Start Rituximab
C - Start IL-6 Receptor Inhibitor
C - Start JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, lung disease-related outcomes (clinical, PFTs, imaging)

68. Should patients with RA who are at target and develop clinical parenchymal lung disease while on MTX continue MTX or switch to alternative DMARD(s)?

P - Patients with RA who are at target and develop parenchymal lung disease while on MTX
I - Continue MTX
C - Switch to alternative csDMARD mono or combination therapy
C - Switch to TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, lung disease outcomes (clinical, PFTs, imaging)

69. Should patients with RA on MTX, who are NOT at target and develop clinical parenchymal lung disease while on MTX, add or switch to alternative DMARD(s)?

P - Patients with RA on MTX, who are not at target and develop clinical parenchymal lung disease while on MTX
I - Add alternative csDMARD mono or combination therapy
C - Switch to alternative csDMARD mono or combination therapy
C - Switch to TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor

O - Disease activity, PROMs, treatment-related harms, lung disease outcomes (clinical, PFTs, imaging)

Congestive Heart Failure

70. Should patients with RA with CHF NYHA class III or IV with inadequate response to csDMARDs add a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?

P - Patients with RA with CHF class III or IV with inadequate response to csDMARDs
I - Add TNF Inhibitor
C - Add Abatacept
C - Add Rituximab
C - Add IL-6 Receptor Inhibitor
C - Add JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

71. Should patients with RA who are at target on a TNF Inhibitor and who develop CHF continue the TNF Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?

P - Patients with RA who are at target on TNF Inhibitor and who develop CHF
I - Continue TNF Inhibitor
C - Switch to Abatacept
C - Switch to Rituximab
C - Switch to IL-6 Receptor Inhibitor
C - Switch to JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, treatment persistence

CANCER

72. Should patients with RA with an inadequate response to csDMARDs, who have had non-melanoma skin cancer, receive a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?

P - Patients with RA with inadequate response to csDMARDs, who have had non-melanoma skin cancer
I - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor

C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, skin cancer recurrence

73. Should patients with RA with inadequate response to csDMARDs, who have had melanoma, receive a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, who have had melanoma
I - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, skin cancer recurrence

74. Should patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder, who have low disease activity, receive csDMARDs or RTX?
P - Patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder, who have low disease activity
I - csDMARDs
C - RTX
O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence

75. Should patients with DMARD-naïve RA who have moderate to high disease activity and a previously treated lymphoproliferative disorder receive csDMARDs or RTX?
P - Patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder who have moderate to high disease activity
I - csDMARDs
C - RTX
O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence

76. Should patients with RA with inadequate response to csDMARDs and a previously treated lymphoproliferative disorder receive RTX or a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs and a previously treated lymphoproliferative disorder
I - RTX
C - Abatacept
C - TNF Inhibitor

C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence

77. Should patients with RA with inadequate response to csDMARDs and a previously treated lymphoproliferative disorder, who are NOT eligible for RTX, receive a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs and a previously treated lymphoproliferative disorder, and who are NOT eligible for RTX
I - JAK Inhibitor
C - Abatacept
C - TNF Inhibitor
C - IL-6 Receptor Inhibitor
O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence

78. Should patients with RA with inadequate response to csDMARD monotherapy and a *remote history (≥ 5 years)* of solid organ cancer and no known residual disease receive triple therapy (MTX or LEF + SSZ + HCQ) or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARD monotherapy and a remote history of solid organ cancer
I - Triple therapy (MTX or LEF + SSZ + HCQ)
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, cancer recurrence

79. Should patients with RA with inadequate response to csDMARD monotherapy with *recently treated (< 5 years)* solid organ cancer receive triple therapy (MTX or LEF + SSZ + HCQ) or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARD monotherapy and recently treated (< 5 years) solid organ cancer
I - Triple therapy
C - TNF Inhibitor
C - Abatacept
C - Rituximab

C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, cancer recurrence

80. Should patients with RA in low disease activity or remission, who are on DMARD(s) and are being treated with a check-point Inhibitor for cancer, stop or continue DMARDs?
P - Patients with RA in low disease activity or remission on DMARD(s), receiving a check-point Inhibitor for cancer
I - Stop DMARDs
C - Continue DMARDs
O - Disease activity, PROMs, treatment-related harms, cancer outcomes
Recommendations may differ for different classes of DMARDs.

81. Should patients with RA with moderate to high disease activity, who are being treated with a check-point Inhibitor for cancer, receive GCs or DMARDs?
P - Patients with RA with moderate to high disease activity receiving a check-point Inhibitor for cancer
I - GCs
C - csDMARDs
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (cancer outcomes)
Recommendations may differ for different doses of GCs and for different classes of DMARDs.

HEPATITIS B

82. Should patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating RTX, undergo frequent monitoring or start prophylactic anti-viral therapy?
P - Patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating RTX
I - Frequent monitoring
C - Prophylactic anti-viral therapy
O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation

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83. Should patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating boDMARD or tsDMARD other than RTX, undergo frequent monitoring or start prophylactic anti-viral therapy?
P - Patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating boDMARD or tsDMARD *other than RTX*
I - Frequent monitoring
C - Prophylactic anti-viral therapy
O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation

84. Should patients with RA and moderate to very high risk of reactivation of Hepatitis B, who are initiating boDMARD or tsDMARDs, undergo frequent monitoring or start prophylactic anti-viral therapy?
P - Patients with RA and moderate to very high risk of reactivation of Hepatitis B, who are initiating boDMARD or tsDMARDs
I - Frequent monitoring
C - Prophylactic anti-viral therapy
O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation

HEPATITIS C

85. Should patients with DMARD-naïve RA and chronic untreated Hepatitis C receive MTX or alternative DMARDs?
P - Patients with DMARD-naïve RA and chronic untreated Hepatitis C
I - MTX
C - Alternative csDMARD mono or combination therapy
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, worsening liver disease (LFTs)

86. Should patients with RA with an inadequate response to csDMARDs, and who have chronic untreated Hepatitis C, receive a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, and who have chronic untreated Hepatitis C

I - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms

Nonalcoholic Fatty Liver Disease (NAFLD) or Nonalcoholic steatohepatitis (NASH)

87. Should patients with RA and NAFLD or NASH receive MTX or alternative DMARDs?
P - patients with DMARD-naïve RA and NAFLD or NASH
I - MTX
C - Alternative DMARDs
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms, worsening liver disease (LFTs)

PRIOR SERIOUS BACTERIAL OR OPPORTUNISTIC INFECTION

88. Should patients with RA with inadequate response to MTX and/or LEF, who have moderate to high disease activity and a prior serious infection within 3 years, add HCQ and SSZ or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to MTX and/or LEF, moderate to high disease activity, and a prior serious infection within 3 years
I - Add SSZ and HCQ
C - Add TNF Inhibitor
C - Add Abatacept
C - Add Rituximab
C - Add IL-6 Receptor Inhibitor
C - Add JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including serious infections)

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89. Should patients with RA with inadequate response to csDMARDs, who have moderate to high disease activity and a prior serious infection within 3 years, receive abatacept or a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, and a prior serious infection within 3 years
I - Abatacept
C - TNF Inhibitor
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including serious infections)

90. Should patients with RA with inadequate response to csDMARDs, who have moderate to high disease activity and a prior serious infection within 3 years, receive low dose GCs (≤ 10mg per day) or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, and a prior serious infection within 3 years
I - Low dose GCs (≤ 10mg/day)
C -TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including serious infections)

91. Should patients with RA with inadequate response to csDMARDs, who have moderate to high disease activity and a prior serious infection within 3 years, on low dose GCs (≤ 10mg per day), receive GCs 11-20mg per day or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, a prior serious infection within 3 years, and on low dose GCs (≤10mg per day)
I - GCs 11-20mg per day
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including serious infections)

ON TREATMENT FOR MAC (Mycobacterium avium complex)

92. Should patients with RA with inadequate response to MTX and/or LEF, who have moderate to high disease activity and are on treatment for MAC, add HCQ and SSZ or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to MTX and/or LEF, moderate to high disease activity, on treatment for MAC
I - Add SSZ and HCQ
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including worsening MAC)

93. Should patients with RA with inadequate response to csDMARDs, who have moderate to high disease activity and are on treatment for MAC, receive a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, on treatment for MAC
I - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including worsening MAC)

94. Should patients with RA with inadequate response to csDMARDs, who have moderate to high disease activity and are on treatment for MAC, receive low dose GCs (≤ 10mg per day) or a boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, on treatment for MAC
I - GCs ≤ 10mg per day
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor

C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including worsening MAC)

95. Should patients with RA with inadequate response to csDMARDs, on low dose GCs (≤ 10mg per day) who have moderate to high disease activity and are on treatment for MAC, receive GCs 11-20mg/day, boDMARD or tsDMARD?
P - Patients with RA with inadequate response to csDMARDs, on low dose GCs (≤ 10mg per day), moderate to high disease activity, on treatment for MAC
I - GCs 11-20mg/day
C - TNF Inhibitor
C - Abatacept
C - Rituximab
C - IL-6 Receptor Inhibitor
C - JAK Inhibitor
O - Disease activity, PROMs, treatment-related harms (including worsening MAC)

VACCINES

96. Should patients with RA, who are on any DMARD except for RTX, receive the influenza vaccine annually in the fall prior to flu season?
P - Patients with RA who are on any DMARD(s) except for RTX
I - Vaccinate with influenza vaccine annually in the fall prior to flu season
C - Do not vaccinate influenza vaccine annually in the fall prior to flu season
O - Influenza, bacterial pneumonia, vaccine associated harms

97. Should patients with RA, who were recently treated with RTX, delay receiving the influenza vaccine?
P - Patients with RA who were recently treated with RTX
I - Delay administering the influenza vaccine (informed based on local flu rates)
C - Do not delay administering the influenza vaccine
O - Influenza, bacterial pneumonia, vaccine associated harms, antibody titers against influenza antigens

98. Should patients with RA on MTX, who are at target, hold MTX for 2 weeks after receiving the influenza vaccine or continue MTX?
P - Patients with RA on MTX who received the influenza vaccine
I - Hold MTX for 2 weeks
C - Continue MTX

0 - Disease activity, PROMS, flare, antibody titers against influenza antigens

99. Should patients with RA on csDMARDs receive live vaccines?
P - Patients with RA on csDMARD
I - Vaccinate with live vaccines
C - Do not vaccinate with live vaccines
O – Vaccine-associated harms

100. Should patients with RA on boDMARDs or JAK Inhibitors receive live vaccines?
P - Patients with RA on boDMARDs or JAK Inhibitors
I - Vaccinate with live vaccines
C - Do not vaccinate with live vaccines
O – Vaccine-associated harms
Recommendations may differ for different vaccines.

101. Should patients with RA on DMARDs receive the recombinant zoster vaccine?
P - Patients with RA on DMARDs
I - Vaccinate with the recombinant zoster vaccine
C - Do not vaccinate with the recombinant zoster vaccine
O – Zoster, vaccine-associated harms
Recommendations may differ for different classes of DMARDs.

102. Should patients with RA on GCs at ≥ 20mg/day for ≥ 14 days receive live vaccines?
P - Patients with RA on GCs at ≥ 20mg/day for ≥ 14 days?
I - Vaccinate with live vaccines at least 1 month after GCs discontinued
C - Do not vaccinate with live vaccines
O – Vaccine-associated harms

Footnotes
- Hierarchy within classes of DMARDs not consistently explicated
- Long-term outcomes: includes treatment persistence
- Short-term glucocorticoids: <=3 months
- Low dose GCs: ≤10mg per day
- At target: As defined by study
- Risk of reactivation of Hepatitis B according to AASLD classification
- Increasing concerns recently regarding potential MTX toxicity because of rising prevalence of NAFLD in the US. Some recommend screening for risk factors, and if present, evaluation by hepatologist

before starting. Main concerns are to ensure no fibrosis. In patients with known NAFLD/NASH consult hepatology before treating. No data/recommendations re: boDMARDs per hepatologists.

- For non-pharmacologic section, all approaches will not be recommended for every patient
- Consider cost