



# AMERICAN COLLEGE OF RHEUMATOLOGY

EDUCATION • TREATMENT • RESEARCH

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

*Project Plan – October 2018*

### **PARTICIPANTS**

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

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

54 **METHODS**

55

56 *Identification of Studies*

57

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

64

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

69

70 *Search Limits*

71

72 Only English language articles will be retrieved.



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73

74 *Grey Literature*

75

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

78

79 *Literature Search Update*

80

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

82

83 *Inclusion/Exclusion Criteria*

84

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

87

88 *Management of Studies and Data*

89

90 References and abstracts will be imported into bibliographic management software (Reference  
91 Manager) (2), duplicates removed, and exported to Distiller SR, a web-based systematic review manager  
92 (3). Screening forms will be created in Distiller SR. Search results will be divided among reviewers, and  
93 two reviewers will screen each title/abstract, with disagreements at the title/abstract screening stage  
94 defaulting to inclusion for full manuscript review. Following the same dual review process,  
95 disagreements at the full manuscript screening stage will be discussed and adjudicated by the literature  
96 review leadership, if necessary.

97

98 *Phases*

99

- 100 1. A search for randomized controlled trials and observational studies about interventions aimed  
101 at the pharmacologic and non-pharmacologic management of RA will be performed to  
102 determine existing studies covering outcomes of interest. Subsequently, identified studies will  
103 be assessed using the RevMan (4) and GRADE Pro tools (5).
- 104 2. Chosen studies will be assessed for risk of bias using modified versions of the Cochrane Risk of  
105 Bias tool (6) and the Newcastle-Ottawa Scale (7).
- 106 3. Additionally, recently published systematic reviews covering outcomes of interest will also be  
107 sought and used for reference cross-checking.

108

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110 *GRADE Methodology*

111

112 GRADE methodology (8) will be used in this project to grade available evidence and facilitate  
113 development of recommendations. The certainty in the evidence (also known as ‘quality’ of evidence)  
114 will be graded as high, moderate, low or very low. The strength of recommendations will be graded as  
115 strong or conditional. The strength of recommendations will not depend solely on the certainty in the  
116 evidence, but also on patient preferences and values, and the weight between benefits and harms. A  
117 series of articles that describe the GRADE methodology can be found on the GRADE working group’s  
118 website: [www.gradeworkinggroup.org](http://www.gradeworkinggroup.org).

119

120 *Analysis and Synthesis*

121

122 The literature review team will analyze and synthesize data from included studies that address the PICO  
123 questions. An evidence profile, including a GRADE Summary of Findings table, will be prepared for each  
124 PICO question using Review Manager (RevMan) (4) and GRADEprofiler (GRADEpro) software (5). The  
125 Summary of Findings table contains the benefits and harms for each outcome across studies, the  
126 assumed and corresponding risk for comparators and interventions (95% CI), the absolute risk and  
127 relative effect (95% CI), the number of participants/number of studies, and the certainty in the evidence  
128 for each critical and important outcome (i.e., high, moderate, low or very low).

129

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

135

136 *Development of Recommendation Statements*

137

138 PICO questions will be revised into drafted recommendation statements. Using the GRADE Evidence  
139 Profiles and Summaries of Findings tables, the voting panel, consisting of eight rheumatologists, one  
140 occupational therapist, one physician assistant, and two patient representatives, will consider the  
141 drafted recommendation statements in two stages. The first assessment will be done individually, and  
142 the results will be anonymous; this vote will only be used to determine where consensus might or might  
143 not already exist and develop the voting panel meeting agenda. At the face-to-face voting panel  
144 meeting, chaired by the principal investigator, the panelists will discuss the evidence in the context of  
145 their clinical experience and expertise to arrive at consensus on the final recommendations. The voting  
146 panel meeting discussions will be supported by the literature review leader, the GRADE expert, and



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147 selected members of the literature review team, who will attend the meeting to provide details about  
148 the evidence, as requested. Voting panel discussions and decisions will be informed by a separately  
149 convened patient panel, which will meet in the days before the voting panel meeting, to provide unique  
150 patient perspectives on the drafted recommendations based on their experiences and the available  
151 literature.

152

153 **PLANNED APPENDICES (AT MINIMUM)**

154

155 A. Final literature search strategies

156 B. GRADE evidence profiles and summary of findings tables for each PICO question

157

158 **AUTHORSHIP**

159

160 Authorship of the guideline will include: principal investigator, Dr. Liana Fraenkel, as the lead author and  
161 voting panel leader; Dr. Elie A. Akl, literature review leader and GRADE expert; Drs. Joan M. Bathon,  
162 Bryant England, and E. William St. Clair, content experts. Members of the literature review team and  
163 voting panel will also be authors. The PI will determine final authorship, dependent on the efforts made  
164 by individuals throughout the guideline development process, using international authorship standards  
165 as guidance.

166

167 **DISCLOSURES/CONFLICTS OF INTEREST**

168

169 The ACR's disclosure and COI policies for guideline development will be followed for this project. These  
170 can be found in the ACR Guideline Manual on [this page of the ACR web site](#), under Policies &  
171 Procedures. *See Appendix B for participant disclosures.*

172

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191 **APPENDIX A – PICO Questions**

192

193 **DMARD = Refers to any csDMARD, boDMARD or tsDMARD**

194

195 **DMARD Groups**

196

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	

197

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

200

201 **INITIAL THERAPY**

202

203 **1. Should patients with DMARD-naïve RA and low disease activity receive MTX monotherapy or an**  
204 **alternative csDMARD monotherapy?**

205 P - Patients with DMARD-naïve RA and low disease activity

206 I - MTX monotherapy

207 C - HCQ

208 C - SSZ

209 C - LEF

210 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

211 **Recommendations may differ for subpopulations with varying risk factors.**

212





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- 213 **2. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX**  
214 **monotherapy or an alternative csDMARD monotherapy?**  
215 P - Patients with DMARD-naïve RA and moderate to high disease activity  
216 I - MTX monotherapy  
217 C - HCQ  
218 C - SSZ  
219 C - LEF  
220 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
221 ***Recommendations may differ for subpopulations with varying risk factors.***  
222  
223 **3. Should patients with DMARD-naïve RA and low disease activity receive csDMARD monotherapy or**  
224 **csDMARD combination (double or triple) therapy?**  
225 P - Patients with DMARD-naïve RA and low disease activity  
226 I - csDMARD monotherapy  
227 C - csDMARD double combination therapy  
228 C - csDMARD triple combination therapy  
229 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
230 ***Recommendations may differ for subpopulations with varying risk factors.***  
231  
232 **4. Should patients with DMARD-naïve RA and moderate to high disease activity receive csDMARD**  
233 **monotherapy or combination (double or triple) therapy?**  
234 P - Patients with DMARD-naïve RA who have moderate to high disease activity  
235 I - csDMARD monotherapy  
236 C - csDMARD double combination therapy  
237 C - csDMARD triple combination therapy  
238 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
239 ***Recommendations may differ for subpopulations with varying risk factors.***  
240  
241 **5. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX**  
242 **monotherapy or boDMARD monotherapy or tsDMARD monotherapy?**  
243 P - Patients with DMARD-naïve RA and moderate to high disease activity  
244 I - MTX monotherapy  
245 C - TNF Inhibitor  
246 C - Abatacept  
247 C - Rituximab  
248 C - IL-6 Receptor Inhibitor  
249 C - JAK Inhibitor



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250 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

251 ***Recommendations may differ for subpopulations with varying risk factors.***

252

253 **6. Should patients with DMARD-naïve RA and moderate to high disease activity receive MTX  
254 monotherapy or boDMARD with MTX or tsDMARD with MTX?**

255 P -Patients with DMARD-naïve RA and moderate to high disease activity

256 I - MTX monotherapy

257 C - TNF Inhibitor + MTX

258 C - Abatacept+ MTX

259 C - Rituximab+ MTX

260 C - IL-6 Receptor Inhibitor+ MTX

261 C - JAK Inhibitor + MTX

262 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

263 ***Recommendations may differ for subpopulations with varying risk factors.***

264

265 **7. Should patients with DMARD-naïve RA and moderate to high disease activity receive mono- or  
266 combination csDMARDs and short-term (< 3 months) GCs or mono or combination csDMARDs alone?**

267 P - Patients with DMARD-naïve RA and moderate to high disease activity

268 I - Mono or combination csDMARDs with short-term (< 3 months) GCs

269 C - Mono or combination csDMARDs alone (i.e., without short-term GCs)

270 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

271 ***Recommendations may differ for different doses of GCs.***

272

273 **8. Should patients with DMARD-naïve RA and moderate to high disease activity, receive long-term (≥  
274 3 months) low dose (≤ 10mg per day) GCs and mono- or combination csDMARDs or mono or  
275 combination csDMARDs alone?**

276 P - Patients with DMARD-naïve RA and moderate to high disease activity

277 I - Mono or combination csDMARDs with long-term (≥ 3 months) low dose (≤ 10mg per day) GCs

278 C - Mono or combination csDMARDs alone (i.e. without long-term GCs)

279 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes

280

281 ***INITIAL ADMINISTRATION OF MTX***

282

283 **9. Should patients with RA initiating MTX receive oral MTX or subcutaneous (SC) MTX?**

284 P - Patients with RA initiating MTX

285 I - Oral MTX

286 C - SC MTX



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- 287 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
288  
289 **10. Should patients with RA initiating MTX receive MTX at 15mg or more per week (includes up-**  
290 **titrating to 15mg over the first month) or less than 15mg per week as the initial dose?**  
291 P - Patients with RA initiating MTX  
292 I - MTX < 15mg per week  
293 C - MTX 15mg per week  
294 C - MTX 20 mg per week  
295 C - MTX 25mg per week  
296 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
297  
298 **11. Should patients with RA initiating oral MTX receive MTX as a single or split dose (over < 24 hours)?**  
299 P - Patients with RA initiating oral MTX  
300 I - MTX single dose  
301 C - MTX split dose  
302 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
303  
304 ***Treat-to-Target (T2T)***  
305  
306 **12. Should patients with RA receive T2T strategies or usual care?**  
307 P - Patients with RA  
308 I - T2T strategy  
309 C - Usual care  
310 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
311  
312 **13. In patients with RA receiving T2T, should the treatment goal be low disease activity or remission?**  
313 P - Patients with RA  
314 I - Treat to low disease activity  
315 C - Treat to remission  
316 O - Disease activity, PROMs, imaging score, treatment-related harms, long-term outcomes  
317  
318 **14. In patients with RA receiving T2T who are NOT at target, should the interval for treatment**  
319 **escalation be 3 months versus less than 3 months after the last DMARD change?**  
320 P - Patients with RA receiving T2T, who have recently added or switched DMARD(s) and are not at target  
321 I - Escalate treatment 3 months or later after the last DMARD change  
322 C - Escalate treatment less than 3 months after the last DMARD change  
323 O - Disease activity, PROMs, treatment-related harms, long-term outcomes



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324

325 **TREATMENT ESCALATION**

326

327 **15. Should patients with RA not tolerating MTX, on folic acid 1 mg/day, increase the dose of folic acid?**

328 P - Patients with RA not tolerating MTX on 1mg of folic acid

329 I - Increase dose of folic acid to > 1mg per day

330 C - Remain on folic acid 1 mg per day

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

332

333 **16. Should patients with RA not tolerating oral MTX receive a split dose (over < 24 hours) or  
334 subcutaneous (SC) MTX?**

335 P - Patients with RA not tolerating oral MTX

336 I - Split oral MTX

337 C - SC MTX

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

339

340 **17. Should patients with RA not tolerating MTX, switch to alternative mono or combination  
341 csDMARDs, to a boDMARD, or to a tsDMARD?**

342 P - Patients with RA not tolerating MTX monotherapy (either oral or SC)

343 I - Switch to non-MTX mono or combination csDMARDs

344 C - Switch to TNF Inhibitor

345 C - Switch to Abatacept

346 C - Switch to Rituximab

347 C - Switch to IL-6 Receptor Inhibitor

348 C - Switch to JAK Inhibitor

349 O - Disease activity, PROMs, treatment-related harms, treatment persistence, long-term outcomes

350

351 **18. Should patients with RA on oral MTX monotherapy 15 mg per week who are NOT at target  
352 increase the dose of oral MTX or switch to SC MTX?**

353 P - Patients with RA on oral MTX monotherapy 15 mg per week who are not at target

354 I - Increase the dose of oral MTX

355 C - Switch to SC MTX

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

357

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



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360 P - Patients with RA on maximally tolerated dose of MTX monotherapy (either oral or SC) who are not at  
361 target

362 I - Add SSZ and HCQ

363 C - Add LEF

364 C - Add TNF Inhibitor

365 C - Add Abatacept

366 C - Add Rituximab

367 C - Add IL-6 Receptor Inhibitor

368 C - Add JAK Inhibitor

369 O - Disease activity, PROMs, treatment-related harms, treatment persistence, long-term outcomes

370

371 **20. Should patients with RA on maximally tolerated dose of LEF monotherapy who are NOT at target,  
372 and have previously failed MTX (due to an inadequate response or adverse events), add SSZ and HCQ,  
373 or add a boDMARD, or add tsDMARD?**

374 P - Patients with RA on maximally tolerated dose of LEF monotherapy who are not at target, and have  
375 previously failed MTX (due to an inadequate response or adverse events)

376 I - Add SSZ and HCQ

377 C - Add TNF Inhibitor

378 C - Add Abatacept

379 C - Add Rituximab

380 C - Add IL-6 Receptor Inhibitor

381 C - Add JAK Inhibitor

382 O - Disease activity, PROMs, treatment-related harms, long-term outcomes

383

384 **21. Should patients with RA on DMARD(s) who are not on GCs and are NOT at target switch to  
385 another DMARD, add a 2nd DMARD, switch to another DMARD and add GCs short-term (< 3 months),  
386 or add both a 2nd DMARD and GCs short-term (< 3 months)?**

387 P - Patients with RA on DMARD(s) not on GCs who are not at target

388 I - Switch to another DMARD

389 C - Add another DMARD

390 C - Switch to another DMARD and add short-term (< 3 months) GCs

391 C - Add another DMARD and add short short-term (< 3 months) GCs

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

393 ***Recommendations may differ for different doses of GCs and for different classes of DMARDs.***

394



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395 **22. Should patients with RA on DMARD(s) not on GCs and NOT at target switch DMARDs, add a 2nd**  
396 **DMARD, switch DMARDs and add GCs *long-term* ( $\geq 3$  months), or add both a 2nd DMARD and GCs**  
397 ***long-term* ( $\geq 3$  months)?**

398 P - Patients with RA on DMARD(s) not on GCs who are not at target

399 I - Switch to another DMARD

400 C - Add another DMARD

401 C - Switch to another DMARD and add long-term ( $\geq 3$  months) GCs

402 C - Add another DMARD and add short long-term ( $\geq 3$  months) GCs

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

404 ***Recommendations may differ for different doses of GCs and for different classes of DMARDs.***

405

406 **23. Should patients with RA on DMARD(s) requiring GCs to remain at target, add a 2nd DMARD or**  
407 **switch to another DMARD to enable tapering off of GCs?**

408 P - Patients with RA on DMARD(s) requiring GCs to remain at target

409 I - No change to management

410 C - Switch to another DMARD

411 C - Add a 2nd DMARD

412 O - Disease activity, PROMs, treatment-related harms, long-term outcomes

413 ***Recommendations may differ for different doses of GCs and for different classes of DMARDs.***

414

415 **24. Should patients with RA on their first TNF Inhibitor who are NOT at target, switch to a 2nd TNF**  
416 **Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?**

417 P - Patients with RA on their first TNF Inhibitor who are not at target

418 I - Switch to a 2nd TNF Inhibitor

419 C - Switch to Abatacept

420 C - Switch to Rituximab

421 C - Switch to IL-6 Receptor Inhibitor

422 C - Switch to JAK Inhibitor

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

424

425 **25. Should patients with RA on their 2nd TNF Inhibitor who are NOT at target, switch to a 3rd TNF**  
426 **Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?**

427 P - Patients with RA on their 2nd TNF Inhibitor who are not at target

428 I - Switching to a 3rd TNF Inhibitor

429 C - Switch to Abatacept

430 C - Switch to Rituximab

431 C - Switch to IL-6 Receptor Inhibitor



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- 432 C - Switch to JAK Inhibitor  
433 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
434  
435 **26. Should patients with RA on their first IL-6 Receptor Inhibitor who are NOT at target, switch to a**  
436 **2nd IL-6 Receptor Inhibitor or switch to a boDMARD targeting a different molecule or to a tsDMARD?**  
437 P - Patients with RA on their first IL-6 Receptor Inhibitor who are not at target  
438 I - Switch to a 2nd IL-6 Receptor Inhibitor  
439 C - Switch to Abatacept  
440 C - Switch to Rituximab  
441 C - Switch to TNF Inhibitor  
442 C - Switch to JAK Inhibitor  
443 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
444  
445 **27. Should patients with RA on their first JAK Inhibitor who are NOT at target, switch to a 2nd JAK**  
446 **Inhibitor or switch to a boDMARD?**  
447 P - Patients with RA on their first JAK Inhibitor who are not at target  
448 I - Switch to a 2nd JAK Inhibitor  
449 C - Switch to Abatacept  
450 C - Switch to Rituximab  
451 C - Switch to TNF Inhibitor  
452 C - Switch to IL-6 Receptor Inhibitor  
453 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
454  
455 ***INTRAARTICULAR (IA) Corticosteroids***  
456  
457 **28. Should patients with RA on DMARDs and synovitis in 1 or 2 joints who are NOT at target receive IA**  
458 **corticosteroids alone or add/switch DMARDs or IA corticosteroids and add/switch DMARD(s)?**  
459 P - Patients with RA on DMARDs with synovitis in 1 or 2 joints who are not at target  
460 I - IA steroids  
461 C - Add DMARD(s)  
462 C - Switch DMARD(s)  
463 C - IA steroids and add DMARD(s)  
464 C - IA steroids and switch DMARD(s)  
465 O - Disease activity, PROMs, treatment-related harms, treatment persistence  
466  
467  
468



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469 ***Recommendations may differ for different classes of DMARDs.***

470

471 ***NON-PHARMACOLOGIC THERAPY vs. DMARDs***

472

473 **29. Should patients with DMARD-naïve RA and low disease activity use any specific diet or DMARDs?**

474 P - Patients with DMARD-naïve RA and low disease activity

475 I - Specific diet

476 C - DMARDs

477 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

478

479 **30. Should patients with DMARD-naïve RA and moderate to high disease activity use any specific diet or DMARDs?**

481 P - Patients with DMARD-naïve RA and moderate to high disease activity

482 I - Specific diet

483 C - DMARDs

484 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

485

486 **31. Should patients with DMARD-naïve RA and low disease activity use any specific nutraceutical or DMARDs?**

488 P - Patients with DMARD-naïve RA and low disease activity

489 I - Specific nutraceutical

490 C - DMARDs

491 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

492

493 **32. Should patients with DMARD-naïve RA and moderate to high disease activity use any specific nutraceutical or DMARDs?**

495 P - Patients with DMARD-naïve RA and moderate to high disease activity

496 I - Specific nutraceutical

497 C - DMARDs

498 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence

499

500 **33. Should patients with DMARD-naïve RA and low disease activity do any specific exercise or take DMARDs?**

502 P - Patients with DMARD-naïve RA and low disease activity

503 I - Specific exercise

504 C - DMARDs

505 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence





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- 506  
507 **34. Should patients with DMARD-naïve RA and moderate to high disease activity do any specific**  
508 **exercise or take DMARDs?**  
509 P - Patients with DMARD-naïve RA and moderate to high disease activity  
510 I - Specific exercise  
511 C - DMARDs  
512 O - Disease activity, PROMs, imaging score, treatment-related harms, treatment persistence  
513  
514 ***NON-PHARMACOLOGIC THERAPY IN ADDITION TO DMARDs***  
515  
516 **35. Should patients with RA on DMARDs use a specific diet?**  
517 P - Patients with RA on DMARDs  
518 I - Specific diet  
519 C - No specific diet  
520 O - Disease activity, PROMs (\*pain and fatigue), treatment-related harms, long term outcomes  
521  
522 **36. Should patients with RA on DMARDs use a specific nutraceutical?**  
523 P - Patients with RA on DMARDs  
524 I - Specific nutraceuticals  
525 C - No specific nutraceuticals  
526 O - Disease activity, PROMs, treatment-related harms, long term outcomes  
527  
528 **37. Should patients with RA on DMARDs use a standardized self-management program?**  
529 P - Patients with RA on DMARDs  
530 I - Standardized self-management program  
531 C - No standardized self-management program  
532 O - Disease activity, PROMs (\*pain and fatigue), arthritis self-efficacy, treatment-related harms, long  
533 term outcomes  
534  
535 **38. Should patients with RA on DMARDs do aerobic exercise?**  
536 P - Patients with RA on DMARDs  
537 I - Aerobic exercise  
538 C - No aerobic exercise  
539 O - Disease activity, PROMs (\*pain and fatigue), treatment-related harms, long term outcomes  
540  
541 **39. Should patients with RA on DMARDs do aquatic exercise?**  
542 P - Patients with RA on DMARDs



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- 543 I - Aquatic exercise  
544 C - No aquatic exercise  
545 O - Disease activity, PROMs (\*pain and fatigue), treatment-related harms, long term outcomes  
546  
547 **40. Should patients with RA on DMARDs do resistance and strengthening exercises?**  
548 P - Patients with RA on DMARDs  
549 I - Resistance and strengthening exercises  
550 C - No resistance or strengthening exercises  
551 O - Disease activity, PROMs (\*pain and fatigue), treatment-related harms, long term outcomes  
552  
553 **41. Should patients with RA and hand/wrist involvement on DMARDs use splinting/orthoses?**  
554 P - Patients with RA and hand/wrist involvement on DMARDs  
555 I - Wrist splinting/orthoses  
556 C - No splinting/orthoses  
557 O - Disease activity, PROMs (\*pain and function), objective measures of hand function, treatment-  
558 related harms, long term outcomes  
559  
560 **42. Should patients with RA and foot/ankle involvement on DMARDs use orthoses?**  
561 P - Patients with RA on DMARDs and foot involvement  
562 I - Orthoses  
563 C - No orthoses  
564 O - Disease activity, PROMs (\*pain and function), treatment-related harms, long term outcomes  
565  
566 **43. Should patients with RA and hand involvement on DMARDs do hand exercises?**  
567 P - Patients with RA and hand involvement on DMARDs  
568 I - Hand exercises  
569 C - No hand exercises  
570 O - Disease activity, PROMs (\*pain and function), objective measures of hand function, treatment-  
571 related harms, long term outcomes  
572  
573 **44. Should patients with RA on DMARDs use joint protection techniques?**  
574 P - Patients with RA on DMARDs  
575 I - Joint protection  
576 C - No joint protection  
577 O - Disease activity, PROMs (\*pain and function), objective measures of function, treatment-related  
578 harms, long term outcomes  
579



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- 580 **45. Should patients with RA on DMARDs use mind-body approaches?**  
581 P - Patients with RA on DMARDs  
582 I - Mind-body approaches  
583 C - No mind-body approaches  
584 O - Disease activity, PROMs (\*pain), arthritis self-efficacy, treatment-related harms, long term outcomes  
585
- 586 **46. Should patients with RA on DMARDs, who are currently employed or want to become employed, use work interventions?**  
587  
588 P - Patients with RA on DMARDs, who are currently employed or want to become employed  
589 I - Work interventions  
590 C - No work interventions  
591 O - Work-related outcomes  
592
- 593 **47. Should patients with RA on DMARDs participate in occupational therapy?**  
594 P - Patients with RA on DMARDs  
595 I - Comprehensive occupational therapy  
596 C - No comprehensive occupational therapy  
597 O - Disease activity, PROMs (\*pain and function), arthritis self-efficacy, objective measure of function,  
598 treatment-related harms, long term outcomes  
599
- 600 **48. Should patients with RA on DMARDs participate in physical therapy?**  
601 P - Patients with RA on DMARDs  
602 I - Comprehensive physical therapy  
603 C - No comprehensive physical therapy  
604 O - Disease activity, PROMs (\*pain and function), arthritis self-efficacy, objective measure of function,  
605 treatment-related harms, long term outcomes  
606
- 607 **49. Should patients with RA on DMARDs who are overweight or obese lose weight?**  
608 P - Patients with RA on DMARDs who are overweight or obese  
609 I - Weight loss  
610 C - No weight loss  
611 O - Disease activity, PROMs (\*pain, fatigue, function, QOL), long term outcomes  
612
- 613 **50. Should patients with RA on DMARDs who are current smokers stop smoking?**  
614 P - Patients with RA on DMARDs  
615 I - Stop smoking  
616 C - Continue smoking



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- 617 O - Disease activity, PROMs (\*pain), long term outcomes  
618  
619 **51. Should patients with RA on DMARDs use acupuncture?**  
620 P - Patients with RA on DMARDs  
621 I - Acupuncture  
622 C - No acupuncture  
623 O - Disease activity, PROMs (\*pain), treatment-related harms, long term outcomes  
624  
625 ***TAPERING OFF (i.e., gradual lowering dose with intent to discontinue)***  
626  
627 **52. Should patients with RA on DMARDs who are in low disease activity taper off DMARDs or not**  
628 **taper off DMARDs?**  
629 P - Patients with RA on DMARDs who are in low disease activity  
630 I - Taper off DMARDs  
631 C - Continue DMARDs at same dose  
632 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target  
633  
634 **53. Should patients with RA on DMARDs who are in remission taper off DMARDs or not taper off**  
635 **DMARDs?**  
636 P - Patients with RA on DMARDs in remission  
637 I - Taper off  
638 C - Continue DMARDs at same dose  
639 O - Disease activity, PROMs, treatment-related harms, time to flare, regain remission  
640  
641 **54. Should patients with RA on DMARDs who are at target taper off DMARDs after 6 months of being**  
642 **at target or after longer than 6 months of being at target?**  
643 P - Patients with RA on DMARDs at target  
644 I - Taper off DMARDs after 6 months of being at target  
645 C - Taper off DMARDs after longer than 6 months of being at target  
646 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target  
647  
648 **55. Should patients with RA on DMARDs and low dose GCs ( $\leq 10$ mg per day) who are at target taper**  
649 **off or continue low dose GCs?**  
650 P - Patients with RA on DMARDs and low dose GCs ( $\leq 10$ mg per day) who are at target  
651 I - Taper off low dose GCs  
652 C - Continue low dose GCs  
653 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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691 ***LOWERING DMARD DOSE (Decrease dose or increase interval and maintain at lower dose)***

692

693 **60. Should patients with RA on DMARD monotherapy who are at target lower the dose or increase**  
694 **the interval between doses or continue the DMARD at the same dose?**

695 P - Patients with RA on DMARD monotherapy in remission

696 I - Continue DMARD at the same dose

697 C - Lower the dose of the DMARD

698 C - Increase the interval between DMARD doses

699 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

700 ***Recommendations may differ for different classes of DMARDs.***

701

702 **61. Should patients with RA on MTX + boDMARD or tsDMARD who are at target continue MTX at the**  
703 **same dose or lower the dose of MTX? (boDMARD or tsDMARD continued at same dose)**

704 P - Patients with RA on MTX + boDMARD or tsDMARD who are at target

705 I - Continue MTX at the same dose

706 C - Lower the dose of MTX

707 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

708

709 **62. Should patients with RA on MTX + boDMARD or tsDMARD who are at target continue the**  
710 **boDMARD or tsDMARD at the same dose or lower the dose or increase the interval between doses of**  
711 **the boDMARD or tsDMARD (MTX continued at same dose)?**

712 P - Patients with RA on MTX + boDMARD or tsDMARD who are at target

713 I - Continue the same dose of the boDMARD or tsDMARD

714 C - Lower the dose of the boDMARD or tsDMARD

715 C - Increase the interval between the doses of the boDMARD or tsDMARD

716 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

717

718 **63. Should patients with RA on MTX + boDMARD or tsDMARD who are at target lower the dose of**  
719 **MTX or lower the dose or increase the interval between doses of the boDMARD or tsDMARD?**

720 P - Patients with RA on MTX + boDMARD or tsDMARD who are at target

721 I - Lower the dose of MTX

722 C - Lower the dose of the boDMARD or tsDMARD

723 C - Increase the interval between doses of boDMARD or tsDMARD

724 O - Disease activity, PROMs, treatment-related harms, time to flare, regain target

725

726 ***ADVERSE EVENT ISSUES***

727



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728 **64. Should patients with RA with (progressive) subcutaneous nodules, who are NOT at target and are**  
729 **not on MTX, start MTX or alternative DMARDs?**

730 P - Patients with RA and (progressive) subcutaneous nodules, who are not at target, are not on MTX

731 I - Start MTX

732 C - Start alternative csDMARD mono or combination therapy

733 C - Start TNF Inhibitor

734 C - Start Abatacept

735 C - Start Rituximab

736 C - Start IL-6 Receptor Inhibitor

737 C - Start JAK Inhibitor

738 O - Disease activity, PROMs, treatment-related harms, nodule progression

739

740 **65. Should patients with RA with (progressive) subcutaneous nodules, who are at target and are on**  
741 **MTX, continue MTX or switch to alternative DMARD(s)?**

742 P - Patients with RA and (progressive) subcutaneous nodules who are at target and are on MTX

743 I - Continue MTX

744 C - Switch to alternative csDMARD mono or combination therapy

745 C - Switch to TNF Inhibitor

746 C - Switch to Abatacept

747 C - Switch to Rituximab

748 C - Switch to IL-6 Receptor Inhibitor

749 C - Switch to JAK Inhibitor

750 O - Disease activity, PROMs, treatment-related harms, nodule progression

751

752 **66. Should patients with RA who have persistent hypogammaglobulinemia after RTX treatment**  
753 **continue RTX or switch to csDMARD mono or combination therapy or to a boDMARD targeting a**  
754 **different molecule or to a tsDMARD?**

755 P - Patients with RA who have persistent hypogammaglobulinemia after RTX treatment

756 I - Continue RTX

757 C - Switch to csDMARD mono or combination therapy

758 C - Switch to TNF Inhibitor

759 C - Switch to Abatacept

760 C - Switch to IL-6 Receptor Inhibitor

761 C - Switch to JAK Inhibitor

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

763

764 ***PARENCHYMAL LUNG DISEASE***



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- 765  
766 **67. Should patients with DMARD-naïve RA who have clinical parenchymal lung disease receive MTX or**  
767 **alternative DMARD(s) for treatment of joint disease?**  
768 P - Patients with DMARD-naïve RA and parenchymal lung disease  
769 I - Start MTX  
770 C - Start alternative csDMARD mono or combination therapy  
771 C - Start TNF Inhibitor  
772 C - Start Abatacept  
773 C - Start Rituximab  
774 C - Start IL-6 Receptor Inhibitor  
775 C - Start JAK Inhibitor  
776 O - Disease activity, PROMs, treatment-related harms, lung disease-related outcomes (clinical, PFTs,  
777 imaging)  
778  
779 **68. Should patients with RA who are at target and develop clinical parenchymal lung disease while on**  
780 **MTX continue MTX or switch to alternative DMARD(s)?**  
781 P - Patients with RA who are at target and develop parenchymal lung disease while on MTX  
782 I - Continue MTX  
783 C - Switch to alternative csDMARD mono or combination therapy  
784 C - Switch to TNF Inhibitor  
785 C - Switch to Abatacept  
786 C - Switch to Rituximab  
787 C - Switch to IL-6 Receptor Inhibitor  
788 C - Switch to JAK Inhibitor  
789 O - Disease activity, PROMs, treatment-related harms, lung disease outcomes (clinical, PFTs, imaging)  
790  
791 **69. Should patients with RA on MTX, who are NOT at target and develop clinical parenchymal lung**  
792 **disease while on MTX, add or switch to alternative DMARD(s)?**  
793 P - Patients with RA on MTX, who are not at target and develop clinical parenchymal lung disease while  
794 on MTX  
795 I - Add alternative csDMARD mono or combination therapy  
796 C - Switch to alternative csDMARD mono or combination therapy  
797 C - Switch to TNF Inhibitor  
798 C - Switch to Abatacept  
799 C - Switch to Rituximab  
800 C - Switch to IL-6 Receptor Inhibitor  
801 C - Switch to JAK Inhibitor





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

803

804

805

806

807 ***Congestive Heart Failure***

808

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

811 P - Patients with RA with CHF class III or IV with inadequate response to csDMARDs

812 I - Add TNF Inhibitor

813 C - Add Abatacept

814 C - Add Rituximab

815 C - Add IL-6 Receptor Inhibitor

816 C - Add JAK Inhibitor

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

818

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

821 P - Patients with RA who are at target on TNF Inhibitor and who develop CHF

822 I - Continue TNF Inhibitor

823 C - Switch to Abatacept

824 C - Switch to Rituximab

825 C - Switch to IL-6 Receptor Inhibitor

826 C - Switch to JAK Inhibitor

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

828

829 ***CANCER***

830

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

834 P - Patients with RA with inadequate response to csDMARDs, who have had non-melanoma skin cancer

835 I - TNF Inhibitor

836 C - Abatacept

837 C - Rituximab

838 C - IL-6 Receptor Inhibitor



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- 839 C - JAK Inhibitor  
840 O - Disease activity, PROMs, treatment-related harms, skin cancer recurrence  
841  
842 **73. Should patients with RA with inadequate response to csDMARDs, who have had melanoma,  
843 receive a TNF Inhibitor or a boDMARD targeting a different molecule or a tsDMARD?**  
844 P - Patients with RA with inadequate response to csDMARDs, who have had melanoma  
845 I - TNF Inhibitor  
846 C - Abatacept  
847 C - Rituximab  
848 C - IL-6 Receptor Inhibitor  
849 C - JAK Inhibitor  
850 O - Disease activity, PROMs, treatment-related harms, skin cancer recurrence  
851  
852 **74. Should patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder,  
853 who have low disease activity, receive csDMARDs or RTX?**  
854 P - Patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder, who have low  
855 disease activity  
856 I - csDMARDs  
857 C - RTX  
858 O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence  
859  
860 **75. Should patients with DMARD-naïve RA who have moderate to high disease activity and a  
861 previously treated lymphoproliferative disorder receive csDMARDs or RTX?**  
862 P - Patients with DMARD-naïve RA with a previously treated lymphoproliferative disorder who have  
863 moderate to high disease activity  
864 I - csDMARDs  
865 C - RTX  
866 O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence  
867  
868 **76. Should patients with RA with inadequate response to csDMARDs and a previously treated  
869 lymphoproliferative disorder receive RTX or a boDMARD targeting a different molecule or a  
870 tsDMARD?**  
871 P - Patients with RA with inadequate response to csDMARDs and a previously treated  
872 lymphoproliferative disorder  
873 I - RTX  
874 C - Abatacept  
875 C - TNF Inhibitor



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- 876 C - IL-6 Receptor Inhibitor  
877 C - JAK Inhibitor  
878 O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence  
879  
880 **77. Should patients with RA with inadequate response to csDMARDs and a previously treated**  
881 **lymphoproliferative disorder, who are NOT eligible for RTX, receive a boDMARD targeting a different**  
882 **molecule or a tsDMARD?**  
883 P - Patients with RA with inadequate response to csDMARDs and a previously treated  
884 lymphoproliferative disorder, and who are NOT eligible for RTX  
885 I - JAK Inhibitor  
886 C - Abatacept  
887 C - TNF Inhibitor  
888 C - IL-6 Receptor Inhibitor  
889 O - Disease activity, PROMs, treatment-related harms, lymphoproliferative disorder recurrence  
890  
891 **78. Should patients with RA with inadequate response to csDMARD monotherapy and a remote**  
892 **history ( $\geq 5$  years) of solid organ cancer and no known residual disease receive triple therapy (MTX or**  
893 **LEF + SSZ + HCQ) or a boDMARD or tsDMARD?**  
894 P - Patients with RA with inadequate response to csDMARD monotherapy and a remote history of solid  
895 organ cancer  
896 I - Triple therapy (MTX or LEF + SSZ + HCQ)  
897 C - TNF Inhibitor  
898 C - Abatacept  
899 C - Rituximab  
900 C - IL-6 Receptor Inhibitor  
901 C - JAK Inhibitor  
902 O - Disease activity, PROMs, treatment-related harms, cancer recurrence  
903  
904 **79. Should patients with RA with inadequate response to csDMARD monotherapy with recently**  
905 **treated ( $< 5$  years) solid organ cancer receive triple therapy (MTX or LEF + SSZ + HCQ) or a boDMARD**  
906 **or tsDMARD?**  
907 P - Patients with RA with inadequate response to csDMARD monotherapy and recently treated ( $< 5$   
908 years) solid organ cancer  
909 I - Triple therapy  
910 C - TNF Inhibitor  
911 C - Abatacept  
912 C - Rituximab



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- 913 C - IL-6 Receptor Inhibitor  
914 C - JAK Inhibitor  
915 O - Disease activity, PROMs, treatment-related harms, cancer recurrence  
916  
917 **80. Should patients with RA in low disease activity or remission, who are on DMARD(s) and are being**  
918 **treated with a check-point Inhibitor for cancer, stop or continue DMARDs?**  
919 P - Patients with RA in low disease activity or remission on DMARD(s), receiving a check-point Inhibitor  
920 for cancer  
921 I - Stop DMARDs  
922 C - Continue DMARDs  
923 O - Disease activity, PROMs, treatment-related harms, cancer outcomes  
924 ***Recommendations may differ for different classes of DMARDs.***  
925  
926 **81. Should patients with RA with moderate to high disease activity, who are being treated with a**  
927 **check-point Inhibitor for cancer, receive GCs or DMARDs?**  
928 P - Patients with RA with moderate to high disease activity receiving a check-point Inhibitor for cancer  
929 I - GCs  
930 C - csDMARDs  
931 C - TNF Inhibitor  
932 C - Abatacept  
933 C - Rituximab  
934 C - IL-6 Receptor Inhibitor  
935 C - JAK Inhibitor  
936 O - Disease activity, PROMs, treatment-related harms (cancer outcomes)  
937 ***Recommendations may differ for different doses of GCs and for different classes of DMARDs.***  
938  
939 ***HEPATITIS B***  
940  
941 **82. Should patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating**  
942 **RTX, undergo frequent monitoring or start prophylactic anti-viral therapy?**  
943 P - Patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating RTX  
944 I - Frequent monitoring  
945 C - Prophylactic anti-viral therapy  
946 O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation  
947



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948 **83. Should patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating**  
949 **boDMARD or tsDMARD other than RTX, undergo frequent monitoring or start prophylactic anti-viral**  
950 **therapy?**

951 P - Patients with RA and low or very low risk of reactivation of Hepatitis B, who are initiating boDMARD  
952 or tsDMARD *other than RTX*

953 I - Frequent monitoring

954 C - Prophylactic anti-viral therapy

955 O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation

956

957 **84. Should patients with RA and moderate to very high risk of reactivation of Hepatitis B, who are**  
958 **initiating boDMARD or tsDMARDs, undergo frequent monitoring or start prophylactic anti-viral**  
959 **therapy?**

960 P - Patients with RA and moderate to very high risk of reactivation of Hepatitis B, who are initiating  
961 boDMARD or tsDMARDs

962 I - Frequent monitoring

963 C - Prophylactic anti-viral therapy

964 O - Disease activity, PROMs, treatment-related harms, Hepatitis B reactivation

965

966 ***HEPATITIS C***

967

968 **85. Should patients with DMARD-naïve RA and chronic untreated Hepatitis C receive MTX or**  
969 **alternative DMARDs?**

970 P - Patients with DMARD-naïve RA and chronic untreated Hepatitis C

971 I - MTX

972 C - Alternative csDMARD mono or combination therapy

973 C - TNF Inhibitor

974 C - Abatacept

975 C - Rituximab

976 C - IL-6 Receptor Inhibitor

977 C - JAK Inhibitor

978 O - Disease activity, PROMs, treatment-related harms, worsening liver disease (LFTs)

979

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

983 P - Patients with RA with inadequate response to csDMARDs, and who have chronic untreated Hepatitis

984 C



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- 985 I - TNF Inhibitor  
986 C - Abatacept  
987 C - Rituximab  
988 C - IL-6 Receptor Inhibitor  
989 C - JAK Inhibitor  
990 O - Disease activity, PROMs, treatment-related harms  
991  
992 ***Nonalcoholic Fatty Liver Disease (NAFLD) or Nonalcoholic steatohepatitis (NASH)***  
993  
994 **87. Should patients with RA and NAFLD or NASH receive MTX or alternative DMARDs?**  
995 P - patients with DMARD-naïve RA and NAFLD or NASH  
996 I - MTX  
997 C - Alternative DMARDs  
998 C - TNF Inhibitor  
999 C - Abatacept  
1000 C - Rituximab  
1001 C - IL-6 Receptor Inhibitor  
1002 C - JAK Inhibitor  
1003 O - Disease activity, PROMs, treatment-related harms, worsening liver disease (LFTs)  
1004  
1005 ***PRIOR SERIOUS BACTERIAL OR OPPORTUNISTIC INFECTION***  
1006  
1007 **88. Should patients with RA with inadequate response to MTX and/or LEF, who have moderate to**  
1008 **high disease activity and a prior serious infection within 3 years, add HCQ and SSZ or a boDMARD or**  
1009 **tsDMARD?**  
1010 P - Patients with RA with inadequate response to MTX and/or LEF, moderate to high disease activity, and  
1011 a prior serious infection within 3 years  
1012 I - Add SSZ and HCQ  
1013 C - Add TNF Inhibitor  
1014 C - Add Abatacept  
1015 C - Add Rituximab  
1016 C - Add IL-6 Receptor Inhibitor  
1017 C - Add JAK Inhibitor  
1018 O - Disease activity, PROMs, treatment-related harms (including serious infections)  
1019



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- 1020 **89. Should patients with RA with inadequate response to csDMARDs, who have moderate to high**  
1021 **disease activity and a prior serious infection within 3 years, receive abatacept or a boDMARD**  
1022 **targeting a different molecule or a tsDMARD?**  
1023 P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, and a  
1024 prior serious infection within 3 years  
1025 I - Abatacept  
1026 C - TNF Inhibitor  
1027 C - Rituximab  
1028 C - IL-6 Receptor Inhibitor  
1029 C - JAK Inhibitor  
1030 O - Disease activity, PROMs, treatment-related harms (including serious infections)  
1031  
1032 **90. Should patients with RA with inadequate response to csDMARDs, who have moderate to high**  
1033 **disease activity and a prior serious infection within 3 years, receive low dose GCs ( $\leq 10$ mg per day) or**  
1034 **a boDMARD or tsDMARD?**  
1035 P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, and a  
1036 prior serious infection within 3 years  
1037 I - Low dose GCs ( $\leq 10$ mg/day)  
1038 C - TNF Inhibitor  
1039 C - Abatacept  
1040 C - Rituximab  
1041 C - IL-6 Receptor Inhibitor  
1042 C - JAK Inhibitor  
1043 O - Disease activity, PROMs, treatment-related harms (including serious infections)  
1044  
1045 **91. Should patients with RA with inadequate response to csDMARDs, who have moderate to high**  
1046 **disease activity and a prior serious infection within 3 years, on low dose GCs ( $\leq 10$ mg per day), receive**  
1047 **GCs 11-20mg per day or a boDMARD or tsDMARD?**  
1048 P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, a prior  
1049 serious infection within 3 years, and on low dose GCs ( $\leq 10$ mg per day)  
1050 I - GCs 11-20mg per day  
1051 C - TNF Inhibitor  
1052 C - Abatacept  
1053 C - Rituximab  
1054 C - IL-6 Receptor Inhibitor  
1055 C - JAK Inhibitor  
1056 O - Disease activity, PROMs, treatment-related harms (including serious infections)



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- 1057  
1058 ***ON TREATMENT FOR MAC (Mycobacterium avium complex)***  
1059  
1060 **92. Should patients with RA with inadequate response to MTX and/or LEF, who have moderate to**  
1061 **high disease activity and are on treatment for MAC, add HCQ and SSZ or a boDMARD or tsDMARD?**  
1062 P - Patients with RA with inadequate response to MTX and/or LEF, moderate to high disease activity, on  
1063 treatment for MAC  
1064 I - Add SSZ and HCQ  
1065 C - TNF Inhibitor  
1066 C - Abatacept  
1067 C - Rituximab  
1068 C - IL-6 Receptor Inhibitor  
1069 C - JAK Inhibitor  
1070 O - Disease activity, PROMs, treatment-related harms (including worsening MAC)  
1071  
1072 **93. Should patients with RA with inadequate response to csDMARDs, who have moderate to high**  
1073 **disease activity and are on treatment for MAC, receive a TNF Inhibitor or a boDMARD targeting a**  
1074 **different molecule or a tsDMARD?**  
1075 P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, on  
1076 treatment for MAC  
1077 I - TNF Inhibitor  
1078 C - Abatacept  
1079 C - Rituximab  
1080 C - IL-6 Receptor Inhibitor  
1081 C - JAK Inhibitor  
1082 O - Disease activity, PROMs, treatment-related harms (including worsening MAC)  
1083  
1084 **94. Should patients with RA with inadequate response to csDMARDs, who have moderate to high**  
1085 **disease activity and are on treatment for MAC, receive low dose GCs ( $\leq 10$ mg per day) or a boDMARD**  
1086 **or tsDMARD?**  
1087 P - Patients with RA with inadequate response to csDMARDs, moderate to high disease activity, on  
1088 treatment for MAC  
1089 I - GCs  $\leq 10$ mg per day  
1090 C - TNF Inhibitor  
1091 C - Abatacept  
1092 C - Rituximab  
1093 C - IL-6 Receptor Inhibitor





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- 1094 C - JAK Inhibitor  
1095 O - Disease activity, PROMs, treatment-related harms (including worsening MAC)  
1096  
1097 **95. Should patients with RA with inadequate response to csDMARDs, on low dose GCs ( $\leq$  10mg per  
1098 day) who have moderate to high disease activity and are on treatment for MAC, receive GCs 11-  
1099 20mg/day, boDMARD or tsDMARD?**  
1100 P - Patients with RA with inadequate response to csDMARDs, on low dose GCs ( $\leq$  10mg per day),  
1101 moderate to high disease activity, on treatment for MAC  
1102 I - GCs 11-20mg/day  
1103 C - TNF Inhibitor  
1104 C - Abatacept  
1105 C - Rituximab  
1106 C - IL-6 Receptor Inhibitor  
1107 C - JAK Inhibitor  
1108 O - Disease activity, PROMs, treatment-related harms (including worsening MAC)  
1109  
1110 **VACCINES**  
1111  
1112 **96. Should patients with RA, who are on any DMARD except for RTX, receive the influenza vaccine  
1113 annually in the fall prior to flu season?**  
1114 P - Patients with RA who are on any DMARD(s) except for RTX  
1115 I - Vaccinate with influenza vaccine annually in the fall prior to flu season  
1116 C - Do not vaccinate influenza vaccine annually in the fall prior to flu season  
1117 O - Influenza, bacterial pneumonia, vaccine associated harms  
1118  
1119 **97. Should patients with RA, who were recently treated with RTX, delay receiving the influenza  
1120 vaccine?**  
1121 P - Patients with RA who were recently treated with RTX  
1122 I - Delay administering the influenza vaccine (informed based on local flu rates)  
1123 C - Do not delay administering the influenza vaccine  
1124 O - Influenza, bacterial pneumonia, vaccine associated harms, antibody titers against influenza antigens  
1125  
1126 **98. Should patients with RA on MTX, who are at target, hold MTX for 2 weeks after receiving the  
1127 influenza vaccine or continue MTX?**  
1128 P - Patients with RA on MTX who received the influenza vaccine  
1129 I - Hold MTX for 2 weeks  
1130 C - Continue MTX



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1131 O - Disease activity, PROMS, flare, antibody titers against influenza antigens

1132

1133 **99. Should patients with RA on csDMARDs receive live vaccines?**

1134 P - Patients with RA on csDMARD

1135 I - Vaccinate with live vaccines

1136 C - Do not vaccinate with live vaccines

1137 O – Vaccine-associated harms

1138

1139 **100. Should patients with RA on boDMARDs or JAK Inhibitors receive live vaccines?**

1140 P - Patients with RA on boDMARDs or JAK Inhibitors

1141 I - Vaccinate with live vaccines

1142 C - Do not vaccinate with live vaccines

1143 O – Vaccine-associated harms

1144 ***Recommendations may differ for different vaccines.***

1145

1146 **101. Should patients with RA on DMARDs receive the recombinant zoster vaccine?**

1147 P - Patients with RA on DMARDs

1148 I - Vaccinate with the recombinant zoster vaccine

1149 C - Do not vaccinate with the recombinant zoster vaccine

1150 O – Zoster, vaccine-associated harms

1151 ***Recommendations may differ for different classes of DMARDs.***

1152

1153 **102. Should patients with RA on GCs at  $\geq 20\text{mg/day}$  for  $\geq 14$  days receive live vaccines?**

1154 P - Patients with RA on GCs at  $\geq 20\text{mg/day}$  for  $\geq 14$  days?

1155 I - Vaccinate with live vaccines at least 1 month after GCs discontinued

1156 C - Do not vaccinate with live vaccines

1157 O – Vaccine-associated harms

1158

1159 ***Footnotes***

1160 • Hierarchy within classes of DMARDs not consistently explicated

1161 • Long-term outcomes: includes treatment persistence

1162 • Short-term glucocorticoids:  $\leq 3$  months

1163 • Low dose GCs:  $\leq 10\text{mg}$  per day

1164 • At target: As defined by study

1165 • Risk of reactivation of Hepatitis B according to AASLD classification

1166 • Increasing concerns recently regarding potential MTX toxicity because of rising prevalence of NAFLD  
1167 in the US. Some recommend screening for risk factors, and if present, evaluation by hepatologist



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- 1168 before starting. Main concerns are to ensure no fibrosis. In patients with known NAFLD/NASH  
1169 consult hepatology before treating. No data/recommendations re: boDMARDs per hepatologists.  
1170 • For non-pharmacologic section, all approaches will not be recommended for every patient  
1171 • Consider cost  
1172  
1173