Objective. To provide guidance to rheumatology providers on the use of coronavirus disease 2019 (COVID-19) vaccines for patients with rheumatic and musculoskeletal diseases (RMDs).

Methods. A task force was assembled that included 9 rheumatologists/immunologists, 2 infectious disease specialists, and 2 public health physicians. After agreeing on scoping questions, an evidence report was created that summarized the published literature and publicly available data regarding COVID-19 vaccine efficacy and safety, as well as literature for other vaccines in RMD patients. Task force members rated their agreement with draft consensus statements on a 9-point numerical scoring system, using a modified Delphi process and the RAND/University of California Los Angeles Appropriateness Method, with refinement and iteration over 2 sessions. Consensus was determined based on the distribution of ratings.

Results. Despite a paucity of direct evidence, 74 draft guidance statements were developed by the task force and agreed upon with consensus to provide guidance for the use of the COVID-19 vaccines in RMD patients and to offer recommendations regarding the use and timing of immunomodulatory therapies around the time of vaccination.

Conclusion. These guidance statements, made in the context of limited clinical data, are intended to provide direction to rheumatology health care providers on how to best use COVID-19 vaccines and to facilitate implementation of vaccination strategies for RMD patients.
INTRODUCTION

The global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused untold disruption to nearly all aspects of human health globally. The substantial morbidity and excess mortality attributed to coronavirus disease 2019 (COVID-19) has had a major impact on health and the delivery of health care. Given the role that rheumatology providers have in serving patients with rheumatic and musculoskeletal diseases (RMDs) (1), particularly those with autoimmune and inflammatory rheumatic diseases (AIRDs), there is an urgent need to optimize strategies to curb the incidence of COVID-19. In addition to preventive measures such as physical distancing, mask-wearing, handwashing, and shelter-in-place orders, the newly available COVID-19 vaccines provide a powerful tool to mitigate the burgeoning growth of adverse outcomes resulting from COVID-19.

Given the leadership role of the American College of Rheumatology (ACR) in facilitating dissemination of high-quality evidence and promoting best practices for the care of RMD patients, the ACR periodically convenes task forces charged with developing methodologically rigorous clinical practice guidelines and guidance documents. Previous ACR guidelines developed for the management of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) have included some information regarding optimal use of vaccines for patients with those conditions. However, because the immunologic principles related to use of vaccines and the impact of vaccine-preventable illnesses on patients cross a broad range of RMDs, the ACR altered its approach in 2020 and convened a new guideline development group to focus exclusively on vaccination. This cross-cutting team was charged with developing encompassing vaccination considerations for all disease and treatment-related areas within rheumatology, rather than embedding them into narrower, disease-specific clinical practice guidelines.

The development process of ACR guidelines follows a rigorous and formal methodology, is based on a reproducible and transparent systematic literature review, incorporates panelist expertise from rheumatology health care professionals and input from related medical experts in other disciplines (e.g., infectious disease, epidemiology), includes direct participation by patients that reflects their values and preferences, and is typically conducted over an extended time frame (e.g., 1 year or longer). In contrast, the ACR develops “guidance” documents when the components needed to develop a formal guideline are not present, e.g., if the need to provide guidance is more urgent than a longer guideline timeline would allow, there is not enough peer-reviewed evidence available to conduct a formal literature review, or when there is very limited expertise and experience, particularly on the part of patients, to help inform the development of recommendations. In these situations, an expert task force is formed to provide the best guidance possible based on the limited information available. The ACR expects that guidance documents will need to be updated with some frequency as new data become available and greater experience is acquired.

Responding to the need to provide timely guidance to practicing clinicians, the ACR COVID-19 Vaccine Guidance Task Force was created as a branch of the ACR Vaccine Guideline effort, to summarize the evidence for newly available COVID-19 vaccines and to make timely clinical recommendations to rheumatology providers for their optimal use. It relied on a limited evidence base derived from clinical trials evaluating the COVID-19 vaccines in non-RMD populations and also included indirect evidence regarding the immunogenicity, clinical effectiveness, and safety of other vaccines administered to RMD patients receiving various immunomodulatory therapies. Armed with this information, task force members were asked to extrapolate across diseases and integrate relevant basic science and immunologic principles to inform the use, timing, and prioritization of the COVID-19 vaccines available in the US and apply them to the care of RMD patients.

Supported by the American College of Rheumatology.

1Jeffrey R. Curtis, MD, MS, MPH: University of Alabama at Birmingham; 2Sindhu R. Johnson, MD, PhD: Toronto Western Hospital, Mount Sinai Hospital, and University of Toronto, Toronto, Ontario, Canada; 3Donald D. Anthony, MD, PhD: Louis Stokes Cleveland VA Medical Center, MetroHealth Medical Center, and Case Western Reserve University, Cleveland, Ohio; 4Reuben J. Arasaratnam, MD: VA North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas; 5Lindsey R. Baden, MD, MSc, Ellen M. Gravallese, MD: Brigham and Women's Hospital, Boston, Massachusetts; 6Anne R. Bass, MD: Hospital for Special Surgery and Weill Cornell Medicine, New York, New York; 7Cassandra Calabrese, DO: Cleveland Clinic, Cleveland, Ohio; 8Rafael Harpaz, MD: Harpaz Herman Consultants, Atlanta, Georgia; 9Rebecca E. Sadun, MD, PhD: Duke University, Durham, North Carolina; 10Amy S. Turner: American College of Rheumatology, Atlanta, Georgia; 11Eleanor Anderson Williams, MD: The Permanente Medical Group, Union City, California; 12Ted R. Mikuls, MD, MSPH: University of Nebraska Medical Center and VA Nebraska-Western Iowa Health Care System, Omaha.

Dr. Curtis has received consulting fees, speaking fees, and/or honoraria from AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Eli Lilly, and Novartis (less than $10,000 each) and from Amgen, Janssen, Pfizer, Myriad, and Sanofi (more than $10,000 each) and research grants from Genentech, Gilead, AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Eli Lilly, Amgen, Janssen, Pfizer, Myriad, and Sanofi. Dr. Johnson has received consulting fees, speaking fees, and/or honoraria from Ikaria and Boehringer Ingelheim (less than $10,000 each) and research grants from Bayer, Boehringer Ingelheim, Corbus, and GlaxoSmithKline. Dr. Baden has received salary support from the New England Journal of Medicine (less than $10,000). Dr. Calabrese has received consulting fees, speaking fees, and/or honoraria from AbbVie and Sanofi Genzyme (less than $10,000 each). Dr. Gravallese has received salary support from the New England Journal of Medicine (more than $10,000). Dr. Mikuls has received consulting fees, speaking fees, and/or honoraria from Sanofi, Horizon, Pfizer, and Gilead (less than $10,000 each) and research support from Bristol Myers Squibb and Horizon. No other disclosures relevant to this article were reported.

Address correspondence to Jeffrey R. Curtis, MD, MS, MPH, University of Alabama at Birmingham, FOT 802, 510 20th Street South, Birmingham, AL 35294. Email: jrcurtis@uabmc.edu.

Submitted for publication February 10, 2021; accepted in revised form March 10, 2021.
METHODS

Convening the ACR COVID-19 Vaccine Guidance Task Force and defining the scope of the clinical guidance. In October 2020, the ACR began assembling the ACR COVID-19 Vaccination Guidance Task Force. Invitations were made following a general solicitation sent to the broad ACR membership seeking interested volunteers. The task force consisted of 13 members from North America and included 9 rheumatologists, 2 infectious disease specialists, and 2 public health experts with current or former employment at the US Centers for Disease Control and Prevention (CDC). Rheumatology task force members were chosen to represent various areas of specialty expertise within the field and to achieve diversity in geographic region, career stage, practice setting, sex, and race/ethnicity, while also ensuring that the majority of task force members had no conflicts of interest. The task force defined the intended scope of the guidance based on input from individual members, and external input was obtained informally from various stakeholders. The process was informed by the previously published ACR Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic (2). The scope of this guidance includes clinically relevant questions that were intended to inform rheumatology patient care related to COVID-19 vaccination and treatment considerations around the time of vaccination. The scope questions were agreed upon by all panel members at an initial teleconference conducted on December 14, 2020.

Developing the evidence summary. The task force was divided into teams that worked in parallel, each charged with summarizing the published literature and other available evidence spanning 4 topics: 1) the efficacy, immunogenicity, and safety data derived from clinical trials of late-stage (i.e., phase III) COVID-19 vaccines ongoing within the US or COVID-19 vaccines already available under the US Food and Drug Administration (FDA) Emergency Use Authorization (EUA); 2) the epidemiology of COVID-19 risk and outcomes in RMD patients; 3) the attenuation of immunogenicity to other vaccines (e.g., influenza, pneumococcal) associated with certain immunomodulatory therapies; and 4) the safety profile (e.g., disease flare, new-onset autoimmune conditions) of non–COVID-19 vaccines in RMD populations. The scoping questions were grouped into these domains and distributed to the teams, which were tasked with gathering and summarizing evidence that addressed the questions within their assigned domains.

The task force agreed that the intended audience for the guidance was rheumatology health care providers managing their individual patients, but they felt that some attention should be directed to a societal perspective, when relevant, around the availability of COVID-19 vaccines and prioritization for individuals with RMDs. The task force took the perspective of developing guidance for a US audience, particularly in view of the fact that the review of COVID-19 vaccine clinical trials was US-focused. Recognizing that RMD patients exhibit high variability with respect to their underlying health conditions, disease severity, treatments, and degree of multimorbidity, these considerations were noted as important facets of individualizing care. Therefore, this guidance was not intended to supersede the judgment of rheumatology care providers nor override the values and perspectives of their patients. Guidance was based on weak and/or indirect evidence and required substantial extrapolation by an expert task force. All statements, therefore, should be considered conditional or provisional. The ACR is committed to updating this guidance document as new evidence emerges.

In the future, the ability to give an additional vaccine booster (if proven necessary or beneficial) will no longer be constrained by limited supplies. Any vaccination strategy is a reasonable compromise in those circumstances. As a practical matter, this tension must be resolved in the context of imperfect prediction as to whether those circumstances may be transient as well as a paucity of scientific evidence. Both individual and societal considerations related to a limited vaccine supply should be considered in issuing vaccine guidance and making policy decisions. Given that context, simplicity should be the touchstone: to avoid confusion, improve implementation, and maintain scientific credibility.

Table 1. Foundational principles, assumptions, and considerations for the guidance statements*

| ACR guidance statements are not intended to supersede the judgment of rheumatology care providers nor override the values and perspectives of their patients. Guidance was based on weak and/or indirect evidence and required substantial extrapolation by an expert task force. All statements, therefore, should be considered conditional or provisional. The ACR is committed to updating this guidance document as new evidence emerges. |
|---|
| The rheumatology community lacks important knowledge on how to best maximize vaccine-related benefits. RMD patients exhibit high variability with respect to their underlying health condition, disease severity, treatments, degree of multimorbidity, and relationship with their specialist provider. These considerations must be considered when individualizing care. |
| There is no direct evidence about mRNA COVID-19 vaccine safety and efficacy in RMD patients. Regardless, there is no reason to expect vaccine harms will trump expected COVID-19 vaccine benefits in RMD patients. |
| The future COVID-19 landscape is uncertain with respect to vaccine effectiveness and safety, uptake, durability, mitigating societal behavior, and emerging viral strain variants. Clinicians nevertheless must act with their best judgment despite this highly uncertain and rapidly changing landscape. |
| The risk of deferring vaccination and thus failing to mitigate COVID-19 risk should be weighed against a possible blunted response to the vaccine if given under suboptimal circumstances. As a practical matter, this tension must be resolved in the context of imperfect prediction as to whether those circumstances may be transient as well as a paucity of scientific evidence. |

To their underlying health conditions, disease severity, treatments, and degree of multimorbidity, these considerations were noted as important facets of individualizing care. Therefore, this guidance was not intended to supersede the judgment of rheumatology care providers nor override the values and perspectives of their patients. Foundational principles, guiding assumptions, and acknowledged limitations were discussed and agreed upon throughout the process (Table 1) and are discussed in this document where most relevant.

Development of the evidence review summary document. Given the accelerated time frame for guidance development, a nonsystematic evidence review was completed and included serial PubMed searches supplemented by postings from the CDC; briefings and other documents available from the FDA, such as dossiers submitted by vaccine manufacturers and transcripts of data presented at the FDA's Vaccines and Related...
Consensus was deemed “strong” when all 13 panel members’ ratings fell within a single tertile (e.g., 7–9, indicative of agreement); all other combinations were considered to reflect “moderate” consensus. A lack of consensus was identified when the median rating fell into the uncertain range (4–6 interval), or more than one-quarter of the ratings fell into the opposite extreme tertile from the median (e.g., ≥4 panelists rated 1–3 [disagree] when the overall median rating was in the 7–9 [agree] range) (14).

**Review and iteration for the ratings of the proposed guidance statements by the task force.** Results from the first round of rating were reviewed and discussed in a task force webinar on January 15, 2021. Discussion was focused on statements for which there was no consensus. Individuals were given the opportunity to comment on all items presented in the initial rating process. Informed by voting results and the group discussion, the task force members refined the wording of several of the rated statements.

Revised statements were sent back to task force members and agreement was again assessed by email, using the same scoring approach described above. Results from the second round of voting were presented to the task force via webinar on January 22, 2021, and minor text revisions were made iteratively in real time until consensus was achieved. A draft manuscript was developed describing the results of the rating process, and all coauthors were given an opportunity to provide direct edits to the document. The ACR Guidance Subcommittee and ACR Quality of Care Committee were given the document in order to provide feedback. It was subsequently sent to the ACR Board of Directors, which approved these recommendations on February 8, 2021. Public vetting of the guidance document was held via an electronic and widely publicized “town hall” held on February 16, 2021 that was open to ACR members and the public, with questions solicited in advance and during the town hall webinar. Finally, given the multitude of uncertainties and evidence gaps considered by the task force, the panel proposed a research agenda of high-impact topics that would advance the science and inform the optimal use of COVID-19 vaccines in RMD patients treated with immunomodulatory therapies. After publication, an ACR project librarian will refresh the specified literature search on a regular basis and submit new articles to the task force for review, and this document will be updated through a similar process as new evidence emerges.

**RESULTS**

Of the 76 guidance statements considered across the 2 rounds of ratings, 74 were rated with a median score of 7, 8, or 9 (i.e., agreement), and 2 of them were not agreed upon. Among the 74 statements achieving agreement, consensus was strong for 16 and moderate for the remainder. One guidance statement related to COVID-19 vaccination in children age <16 years was rated with a median value of 5 (uncertain) by the task force, in...
part reflecting the desire to obtain more feedback from pediatric rheumatology providers. Additional input was therefore sought from the ACR Pediatric Rheumatology Clinical Guidance Task Force. This task force recognized the practical considerations related to the lack of any COVID-19 vaccine being currently available in the US under an FDA EUA for children younger than age 16 years, although it recognized that ≥1 COVID vaccine clinical trial has enrolled patients as young as age 12 years (ClinicalTrials.gov identifiers: NCT04649151 and NCT04388728) (16,17). It also acknowledged a dearth of evidence in children with RMDs regarding both the epidemiology of COVID-19 and the resulting complications. Therefore, the Pediatric Task Force recommended to await additional evidence from clinical trials regarding the safety and effectiveness of COVID-19 vaccination in children before providing formal guidance statements, with the expectation that once such evidence becomes available, this topic will be revisited. The second statement for which the task force was unable to reach consensus relates to vaccination in the context of ongoing treatment with high-dose glucocorticoids, discussed in detail below.

**General considerations related to vaccination against COVID-19 in patients with RMDs.** Twelve guidance statements related to general considerations of COVID-19 vaccination in RMD patients achieved consensus (Table 2). Statements were descriptively categorized into ≥1 domain to facilitate ease of reference. The panel concurred that rheumatology health care providers were responsible for engaging RMD patients in discussions to assess whether they had been vaccinated against COVID-19 and to document related details (e.g., which vaccine had been administered, timing of vaccination, whether the series had been completed). For those not vaccinated, and similar to other vaccination guidelines for immunocompromised patients such as those from the Infectious Disease Society of America, it was thought that the rheumatology provider should share responsibility with the patient's primary care provider (when available) to ensure appropriate vaccinations are administered (18,19). Rheumatology providers should also engage patients in a shared decision-making process to discuss the following: their attitudes, intent, and concerns related to vaccination; local incidence of COVID-19; individual circumstances (e.g., disease activity, medications, comorbidities) that may affect risk; ability to adhere to nonpharmacologic public health interventions; and vaccine efficacy and potential safety concerns (e.g., local or systemic reactogenicity, potential for disease worsening or flare).

The epidemiology of viral infection risk in RMD patients, and specifically, the risk for infection due to SARS–CoV-2, was then discussed. For this topic, the task force elected to narrow the scope of the patient population under consideration and define a presumably

| Table 2. General considerations related to COVID-19 vaccination in patients with RMD* |
|---------------------------------------------------------------|
| **Statement domain, guidance no.** | **Guidance statement** | **Level of task force consensus** |
| Clinical practice, 1 | The rheumatology health care provider is responsible for engaging the RMD patient in a discussion to assess COVID-19 vaccination status. | Strong |
| Clinical practice, 2 | The rheumatology health care provider is responsible for engaging the RMD patient in a shared decision-making process to discuss receiving the COVID-19 vaccine. | Moderate |
| Epidemiology, 3 | AIIRD patients are at higher risk for incident viral infections compared to the general population. | Moderate |
| Epidemiology, 4 | After considering the influence of age and sex, AIIRD patients are at higher risk for hospitalized COVID-19 compared to the general population. | Moderate |
| Epidemiology, 5 | Acknowledging heterogeneity due to disease- and treatment-related factors, AIIRD patients have worse outcomes associated with COVID-19 compared to the general population of similar age and sex. | Moderate |
| Epidemiology, 6 | Across AIIRD conditions, and within any specific disease, there is substantial variability in disease- and treatment-related risk factors for COVID-19 that may put some patients at higher risk than others.† | Moderate |
| Public health, 7 | Based on increased risk for COVID-19, AIIRD patients should be prioritized for vaccination before the nonprioritized general population of similar age and sex. | Moderate |
| Vaccine safety, 8 | Beyond known allergies to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients. | Moderate |
| Vaccine effectiveness, 9 | The expected response to COVID-19 vaccination for many AIIRD patients receiving systemic immunomodulatory therapies is likely to be blunted in its magnitude and duration compared to the general population. | Moderate |
| Disease-related, 10 | As a general principle, vaccination should optimally occur in the setting of well-controlled AIIRD. | Moderate |
| Disease-related, 11 | A theoretical risk exists for AIIRD flare or disease worsening following COVID-19 vaccination. | Moderate |
| Vaccine safety, 12 | The benefit of COVID-19 vaccination for RMD patients outweighs the potential risk for new-onset autoimmunity. | Moderate |

* COVID-19 = coronavirus disease 2019; RMD = rheumatic and musculoskeletal disease.
† For examples of these autoimmune and inflammatory rheumatic disease (AIIRD) conditions, see Supplementary Table 1, on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.41734/abstract.
higher-risk subgroup of patients with RMDs. Some RMD conditions would include those managed by rheumatology providers but not generally associated with high levels of systemic inflammation (e.g., osteoarthritis, fibromyalgia, osteoporosis) and for which conventional, biologic, or targeted synthetic disease-modifying antirheumatic drugs (DMARDs) or other therapies with immunosuppressive effects are typically not indicated. The patient population was thus restricted to those with AIIRDs (see Supplementary Table 1 for definitions, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41734/abstract). Among these individuals, the risk for incident viral infections (e.g., herpes zoster) was rated as being higher than for the general population (20–22). There was also agreement that AIIRD patients are likely to be at increased risk for hospitalized SARS–CoV-2 infection (23–27) and that age, race/ethnicity (especially for underrepresented minorities), and sex were important risk factors that needed to be considered (28–31) in evaluating risk at the individual patient level.

Multimorbidity was felt to likewise play an important role in the risk for developing COVID-19. While some population-based epidemiologic studies of COVID-19 incidence and outcomes in AIIRD patients have controlled for general multimorbidity or specific comorbidities (23,24,32), the panel recognized that some comorbidities that increase infection risk were shared risk factors for development of AIIRDs (e.g., smoking and related pulmonary conditions associated with incident RA). These may represent direct manifestations such as interstitial lung disease associated with some AIIRDs, or they could be downstream sequelae causally related to the underlying inflammatory processes of AIIRDs or their treatment (e.g., premature and advanced atherosclerotic vascular disease in systemic lupus erythematosus patients; obesity, diabetes, and features of the metabolic syndrome in psoriatic arthritis patients; or those receiving long-term glucocorticoids). For that reason, adjustment for these comorbidities might be inappropriate and would underestimate the risk of COVID-19 infection in patients with AIIRDs. Therefore, age- and sex-adjusted risk estimates were preferred by some task force members when comparing risk and outcomes of COVID-19 in AIIRD patients to the general population.

The few large population-based studies of COVID-19 incidence and outcomes in AIIRD patients had minimal demographic diversity, and therefore race/ethnicity could not be easily evaluated as an independent risk factor. Finally, the panel acknowledged challenges in being able to disentangle the independent role of the disease activity and severity of various AIIRDs from the medications used to treat them (e.g., higher-dose glucocorticoids [33]), so-called confounding by severity, as risk factors for worse COVID-19 outcomes.

Despite these important methodologic caveats and acknowledged limitations in the evidence base, AIIRD patients were rated as having worse outcomes (e.g., need for intensive care unit [ICU] treatment, mechanical ventilation, persistent infection, death) following COVID-19 compared to patients of similar age and sex without such conditions (23–27,34). In terms of the policy implications of this reasoning, the task force agreed that in general, AIIRD patients should be prioritized to be allocated to receive vaccination before the nonprioritized general population of similar age and sex (35). The panel recognized important heterogeneity across AIIRD conditions, such that (for example) an RA patient with quiescent disease treated only with hydroxychloroquine likely has a lower risk for COVID-19 and adverse outcomes compared to a vasculitis patient with very active disease treated with intravenous (IV) cyclophosphamide or rituximab (RTX) and high-dose glucocorticoids (31), although the protection conferred by COVID-19 vaccination may also differ greatly.

Turning attention to vaccination of individual patients, the task force felt that there were no additional known contraindications to receipt of the COVID-19 vaccine other than known allergies to vaccine components as stipulated by guidance from the CDC (36). Extrapolating evidence derived from studies of other vaccines, the expected response to vaccination in many AIIRD patients receiving certain systemic immunomodulatory therapies was deemed likely to be blunted, albeit with uncertain diminution in either the magnitude or duration of response compared to the general population (36,37). The task force acknowledged a complete absence of direct evidence supporting this assertion and placed great importance on prioritizing this topic as part of a future research agenda. The timing of vaccination was considered more ideal in the setting of well-controlled disease, yet the task force noted that patients and their providers should not be dissuaded from vaccination under less-than-ideal conditions, with additional timing considerations as discussed below.

Based on data derived from the published literature, a potential risk for a flare of the patient’s underlying AIIRD following vaccination was acknowledged. For example, based on randomized controlled trial data (38), the frequency of flare was higher in RA patients randomized to have methotrexate (MTX) withheld at the time of influenza vaccination compared to those randomized to continue (10.6% versus 5.1%, respectively), with flare defined as an increase in the Disease Activity Score in 28 joints (DAS28) of >1.2, or >0.6 if the baseline DAS28 was ≥3.2 (39). A subsequent pooled analysis that included that trial and another showed that while the mean change in DAS28 did not differ between groups, the adjusted flare rate in the 2-week withhold group (MTX withhold) was 2.90-fold higher (95% confidence interval 0.96–4.56; P = 0.063) compared to the group that continued MTX (MTX continue), with a difference in proportions experiencing flare of 10.8% (MTX withhold group) versus 5.8% (MTX continue group) (38,40–42). This risk of flare or disease worsening was catalogued as an important topic slated for the future research agenda. Finally, although some new-onset AIIRDs (e.g., RA, vasculitis) or flares of preexisting AIIRDs have been reported after COVID-19 in published case reports (43,44), the expected benefit of vaccination for AIIRD patients was thought to outweigh any theoretical risk for the development of new-onset autoimmune conditions or other potentially
immune-mediated manifestations or abnormalities (e.g., Bell’s palsy, Guillain-Barré syndrome, anti-RNA antibodies in systemic lupus erythematosus patients, immune thrombocytopenic purpura) following vaccination.

### Indications for vaccination and timing considerations.

As summarized in Table 3, and consistent with guidance from the CDC for the general US population, the panel recommended that RMD and AIIRD patients be offered and receive vaccination against SARS-CoV-2. Discussion was held regarding the age cut-off for vaccination, and the panel agreed that guidance should be made consistent with the EUA of available vaccines (i.e., age ≥16 years as of January 2021), with the potential for that cutoff to change in the future based on future revisions to EUAs for existing vaccines, forthcoming EUAs for new vaccines, or age restrictions applicable to FDA licensure.

### Table 3. Recommendations for use of the COVID-19 vaccine in RMD patients*

| Statement domain, guidance no. | Guidance statement | Level of task force consensus |
|-------------------------------|-------------------|------------------------------|
| Clinical practice, 13 | RMD patients should be offered COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.† | Strong |
| Clinical practice, 14 | RMD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.† | Moderate |
| Clinical practice, 15 | AIIRD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.† | Moderate |
| Clinical practice, 16 | RMD patients without an AIIRD who are receiving immunomodulatory therapy should be vaccinated in a similar manner as described in this guidance as AIIRD patients receiving those same treatments. | Moderate |
| Vaccine effectiveness/safety, 17 | Based on the data for the mRNA COVID-19 vaccines available in the US, there is no preference for one COVID-19 vaccine over another. Therefore, AIIRD patients should receive either vaccine available to them. | Moderate |
| Vaccine effectiveness, 18 | For a multidose vaccine, AIIRD patients should receive the second dose of the same vaccine, even if there are nonserious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines (30). | Strong |
| Clinical practice, 19 | Health care providers should not routinely order any laboratory testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 postvaccination, nor to assess the need for vaccination in an as-yet-unvaccinated person. | Strong |
| Public health, 20 | Following COVID-19 vaccination, RMD patients should continue to follow all public health guidelines regarding physical distancing and other preventive measures. | Strong |
| Clinical practice/public health, 21 | Household members and other frequent close contacts of AIIRD patients should undergo COVID-19 vaccination when available to them to facilitate a "cocooning effect" that may help protect the AIIRD patient. No priority for early vaccination is recommended for household members. | Moderate |
| Vaccine effectiveness/disease-related, 22 | Except for AIIRD patients with life-threatening disease (e.g., in the ICU for any reason), COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity. | Strong |
| Vaccine effectiveness/disease-related, 23 | In AIIRD patients with life-threatening disease (e.g., in the ICU for any reason), COVID-19 vaccination should be deferred until their disease is better controlled. | Moderate |
| Vaccine effectiveness/disease-related, 24 | AIIRD patients with active but non-life-threatening disease should receive COVID-19 vaccination. | Strong |
| Vaccine effectiveness/disease-related, 25 | AIIRD patients with stable or low disease activity AIIRDs should receive COVID-19 vaccination. | Strong |
| Vaccine effectiveness/disease-related, 26 | AIIRD patients not receiving immunomodulatory treatments should receive the first dose of the COVID-19 vaccine prior to initiation of immunomodulatory therapy when feasible. | Moderate |

* COVID-19 = coronavirus disease 2019; RMD = rheumatic and musculoskeletal disease; EUA = Emergency Use Authorization; FDA = US Food and Drug Administration; AIIRD = autoimmune and inflammatory rheumatic disease; CDC = Centers for Disease Control and Prevention; ICU = intensive care unit.
† Age ≥16 years as of January 2021.
Recommendations on which patients should be vaccinated were extended to patients with RMDs who did not have conditions typically considered to be AIIRDs but for which immunomodulatory or DMARD therapies might be used off-label. For example, patients with erosive osteoarthritis might receive MTX, or gout patients treated with pegloticase might be concomitantly treated with MTX to reduce pegloticase immunogenicity. These circumstances, in which MTX or another immunomodulatory therapy is being used for a non-AIIRD condition, would be treated synonymously with the guidance for MTX offered in this document. However, within the category of patients with AIIRDs and/or those receiving immunomodulatory therapies, substantial heterogeneity of disease- and treatment-related risk factors was noted. Some AIIRD patients were expected to be at higher risk for infection and morbidity than others, and thus the impetus for COVID-19 vaccination might be stronger for some individual patients or patient groups (e.g., patients with systemic lupus erythematosus receiving cytotoxic therapy and higher-dose glucocorticoids, or patients receiving RTX therapy), although the vaccine might be less effective in these same individuals.

Extensive discussion was held regarding whether consideration for a particular vaccine, or vaccine platform (e.g., messenger RNA [mRNA] versus adenoviral vector) might be preferred in general or for selected patients. However, given that the majority of the data available were for 2 mRNA vaccines, and the future evidence base and availability of alternative vaccine platforms was uncertain, the task force restricted its consideration to only the 2 mRNA vaccines available in the US at the time of deliberation. With this in mind, there was no preference for one COVID-19 vaccine over another, and RMD patients undergoing vaccination were recommended to receive whichever of the mRNA vaccines was available to them. The task force noted that none of the SARS-CoV-2 vaccine candidates in development would be classified as a canonical live-virus vaccine, including the adenoviral vector-based vaccines which are replication-deficient (45). Thus, the usual prohibitions against the use of live-virus vaccines in immunosuppressed patients does not apply. High importance was placed on updating this guidance document as additional data emerge for new vaccines yet to be licensed or available in the US under an EUA.

The task force also noted the CDC guidance regarding recommendation against routine prevaccine prophylaxis with acetaminophen or nonsteroidal antiinflammatory drugs to prevent postvaccination symptoms, which states, “[R]outine prophylactic administration of these medications for the purpose of preventing postvaccination symptoms is not currently recommended, because information on the impact of such use on COVID-19 vaccine-induced antibody responses is not available at this time” (46). However, the CDC has made no prohibition against their use for patients who experience local or systematic symptoms postvaccination.

Following receipt of the first dose in a vaccine series, patients were recommended to receive the second dose of the same type of vaccine, assuming no contraindication to the second dose per CDC guidance (e.g., a severe allergic reaction, or an immediate allergic reaction of any severity to the vaccine or any of its components, including polyethylene glycol) (46). Persons who develop SARS-CoV-2 infection between the first and second dose of a 2-dose vaccine series should delay the second dose until they have recovered from the acute illness (if symptomatic) and discontinued isolation, and then they should receive the second dose without delay (46). Consistent with CDC guidance (36), SARS-CoV-2–infected patients who received monoclonal antibodies (e.g., bamlanivimab, casirivimab, imdevimab) or convalescent plasma as part of treatment for COVID-19 should defer vaccination for ≥90 days following receipt of antibody therapy.

Thus far, there is no proven laboratory-based immune correlate of protection against SARS-CoV-2 following natural infection or vaccination. Moreover, some commercially available SARS-CoV-2 serologic assays do not detect antibody responses to spike protein generated by the currently available mRNA vaccines, but rather measure antibodies to nucleocapsid protein. Therefore, the task force recommended that health care providers not do any of the following: routinely order laboratory testing to assess the need for vaccination in an unvaccinated person, screen for asymptomatic SARS-CoV-2 shedding, or assess SARS-CoV-2 immunity following vaccination. The task force expressed strong interest in modifying this guidance once additional data evolve regarding the potential utility of laboratory-based testing which that might be helpful in select patients. Household members and other frequent close contacts of AIIRD patients were recommended to undergo COVID-19 vaccination when available, in order to facilitate a “cocooning effect” that may help protect at-risk AIIRD patients. However, the priority for vaccination for these close contacts should not be elevated for this reason.

A series of statements was rated by the panel with respect to the general timing of COVID-19 vaccination in relation to AIIRD disease activity, again acknowledging a dearth of direct evidence. Except for those with severe and life-threatening illness (e.g., a hospitalized patient receiving treatment in the ICU for any condition), vaccination was recommended irrespective of disease activity and severity. Even for ICU-treated patients for whom vaccination was recommended to be deferred for a short time, the task force felt that when the patient was well enough to be discharged from the hospital, vaccination would likely be appropriate. Acknowledging a balance between vaccinating and obtaining a blunted but still modest response, and the duty to allocate vaccine resources toward the settings in which they are likely to have the greatest benefit, the panel identified this scenario as an important evidence gap. For AIIRD patients in other settings, including those with either active but non-life-threatening disease, and certainly for patients with stable and/
Table 4.  Guidance related to the timing of COVID-19 vaccination in relation to use of immunomodulatory therapies in RMD patients*  

| Medication(s) | COVID-19 vaccine administration timing considerations | Level of task force consensus |
|---------------|------------------------------------------------------|-----------------------------|
| Hydroxychloroquine; sulfasalazine; leflunomide; apremilast; IVIG | Do not delay or adjust vaccine administration timing. | Strong |
| Methotrexate; mycophenolate mofetil; azathioprine; cyclophosphamide (IV or oral); TNFi; IL-6R; IL-1Ra; IL-17; IL-12/IL-23; IL-23; belimumab; JAK inhibitors; abatacept (IV or SC); oral calcineurin inhibitors; GCs (prednisone-equivalent dose <20 mg/day) † | Do not delay or adjust vaccine administration timing. | Moderate |
| Rituximab | Assuming that a patient’s COVID-19 risk is low or able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated ~4 weeks prior to next scheduled rituximab cycle. | Moderate |

* COVID-19 = coronavirus disease 2019; RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; TNFi = tumor necrosis factor inhibitor; SC = subcutaneous.
† Examples of cytokine and kinase inhibitors include the following: for interleukin-6 receptor (IL-6R), sarilumab and tocilizumab; for IL-1 receptor antagonist (IL-1Ra), anakinra and canakinumab; for IL-17, ixekizumab and secukinumab; for IL-12/IL-23, ustekinumab; for IL-23, guselkumab and rizankizumab; for JAK inhibitors, baricitinib, tofacitinib, and upadacitinib. Consensus was not reached for patients receiving glucocorticoids (GCs) at prednisone-equivalent doses of ≥20 mg/day.

or low disease activity, vaccination was recommended. Finally, patients naive to or not currently receiving immunomodulatory therapies were recommended to receive their first dose of vaccine without delay. Additional considerations for medication timing were subsequently discussed.

**Treatment-specific timing of vaccination.** Guidance regarding optimizing the timing of COVID-19 vaccination in relation to the use of various immunomodulatory therapies is provided in Table 4. There was recognition that the ability to carefully time COVID-19 vaccination is sometimes limited in a real-world setting, and the overarching view was that COVID-19 vaccination should be given rather than not given if timing in relation to immunomodulatory drugs is not under the provider’s or patient’s control.

Strong consensus was achieved regarding the statement to not delay COVID-19 vaccination for patients receiving hydroxychloroquine, sulfasalazine, leflunomide, apremilast, or IV immunoglobulin (10,47). A similar recommendation with moderate consensus was achieved for most of the remaining immunomodulatory therapies considered (48–59). One exception was RTX (10,11,60–64), for which the panel recommended to schedule vaccination such that the vaccine series would be initiated ~4 weeks prior to the next scheduled RTX dose. For example, a patient receiving RTX as a 2-dose cycle (spaced 2 weeks apart), with cycles repeating every 6 months, would be recommended to initiate vaccination ~5 months after the start of the prior RTX cycle. RTX dosing could then be resumed 2–4 weeks after the second COVID-19 vaccination, as discussed in the next section. Those receiving RTX cycles at 4-month intervals would initiate vaccination 3 months after the prior RTX cycle. In order to follow this recommendation, the task force invoked the assumption that a patient’s COVID-19 risk was low or able to be mitigated by preventive health measures. The rationale for this recommendation comes from a single study demonstrating minimal response to influenza vaccination in 11 patients vaccinated 4–8 weeks after RTX treatment, with modestly restored responses in patients vaccinated 6–10 months after their last RTX dose (65).

As the second statement for which consensus was not achieved, the panel was uncertain about whether to delay vaccine if an AIIRD patient was receiving glucocorticoids at a prednisone-equivalent dose of ≥20 mg per day. Controversy stemmed as to whether vaccine response might be blunted in this circumstance, which may relate to the glucocorticoids themselves or to the presumably high disease activity and severity (66,67). Other factors discussed include the disease being treated and the medical management considerations if the patient were to manifest systemic reactogenicity (e.g., persistent high fever). Concern regarding an attenuated response to the vaccine in this circumstance would be partially mitigated if there was a possibility to later order serologies or other laboratory tests, and clinicians were able to assess vaccine-induced immunity and administer a booster or revaccinate if needed. However, such laboratory-based correlates of protection are not currently available, and the task force did not expect that the opportunity to revaccinate would be readily at hand.

**Use and timing of immunomodulatory therapies in relation to COVID-19 vaccination administration.** No evidence was found to support concern regarding the use or timing of immunomodulatory therapies in relation to vaccine safety, and guidance regarding medication timing (Table 5) was therefore given in light of the intent to optimize vaccine response. For most therapies, the task force recommended that no changes be made with respect to interrupting or otherwise optimizing the timing of immunomodulatory therapy (10,68,69). For MTX, however, the panel recommended that MTX be withheld 1 week after each...
In contrast, the panel recommended that subcutaneous abatacept (ABA) be withheld for both 1 week before and 1 week after the first dose of the vaccine (i.e., a total of 2 weeks) but not withheld for the second dose (53). This recommendation was made in light of several studies suggesting a negative effect of ABA on vaccine immunogenicity (10,70,71,77–79). The additional rationale for withholding ABA around the time of the first vaccine dose, but not the second, was that the first vaccine dose primes naive T cells, naive T cell priming is inhibited by CTLA-4, and ABA is a CTLA-4 Ig construct. This consideration relates to the fact that the COVID-19 vaccine provides protection against a novel infectious agent, in contrast to most other vaccines which generally function by reactivating memory T cells. CTLA-4 should not, however, inhibit “boosts” of already primed T cells at the time of the second vaccine dose. This principle would theoretically also apply to subsequent booster doses of vaccine, should future evidence suggest that these are needed or beneficial in some patients.

Additionally, as with MTX, the practical considerations surrounding guidance to withhold subcutaneous ABA for a total of 2 weeks around each of the 2 vaccine doses (4 weeks total) was raised as a concern. Following similar immunologic principles, the panel recommended to time IV ABA administration (typically every 4 weeks) so that the first vaccine dose would occur 4 weeks after ABA infusion (i.e., the entire dosing interval), and postpone the subsequent ABA infusion by 1 week (i.e., a 5-week gap in total); no medication adjustments for the second vaccine dose. For patients receiving IV abatacept, the panel recommended to time IV ABA administration (typically every 4 weeks) so that the first vaccine dose would occur 5 weeks following the previous dose. For some patients.

Table 5. Guidance related to the use and timing of immunomodulatory therapies in relation to COVID-19 vaccination administration in RMD patients*

| Medication(s) | Immunomodulatory therapy timing considerations | Level of task force consensus |
|---------------|---------------------------------------------|-------------------------------|
| Hydroxychloroquine; apremilast; IVIG; GCs (prednisone-equivalent dose <20 mg/day) | No modifications. | Strong |
| Sulfasalazine; leflunomide; mycophenolate mofetil; azathioprine; cyclophosphamide (oral); TNFi; IL-6R; IL-1Ra; IL-17; IL-12/IL-23; IL-23; belimumab; oral calcineurin inhibitors; GCs (prednisone-equivalent dose ≥20 mg/day)† | No modifications. | Moderate |
| Methotrexate | Withhold methotrexate 1 week after each vaccine dose, for those with well-controlled disease. | Moderate |
| JAK inhibitors† | Withhold JAK inhibitors for 1 week after each vaccine dose. | Moderate |
| Abatacept (SC) | Withhold abatacept both 1 week prior to and 1 week after the first COVID-19 vaccine dose only; no interruption around the second vaccine dose. | Moderate |
| Abatacept (IV) | Time administration so that the first vaccination will occur 4 weeks after abatacept infusion (i.e., the entire dosing interval), and postpone the subsequent abatacept infusion by 1 week (i.e., a 5-week gap in total); no medication adjustments for the second vaccine dose. | Moderate |
| Cyclophosphamide (IV) | Time cyclophosphamide administration so that it will occur ~1 week after each vaccine dose, when feasible. | Moderate |
| Rituximab | Delay rituximab 2–4 weeks after second vaccine dose if disease activity allows. | Moderate |

* Guidance to withhold a therapy was made based on the assumption that the patient had well-enough controlled disease to allow for a temporary interruption; if not, decisions should be made on a case-by-case basis considering the circumstances involved. COVID-19 = coronavirus disease 2019; RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; GCs = glucocorticoids; TNFi = tumor necrosis factor inhibitor; SC = subcutaneous.
† Examples of cytokine and kinase inhibitors include the following: for interleukin-6 receptor (IL-6R), sarilumab and tocilizumab; for IL-1 receptor antagonist (IL-1Ra), anakinra and canakinumab; for IL-17, ixekizumab and secukinumab; for IL-12/IL-23, ustekinumab; for IL-23, guselkumab and rizankizumab; for JAK inhibitors, baricitinib, tofacitinib, and upadacitinib.
was made to coordinate timing so that cyclophosphamide infusion occurs ~1 week after each vaccine dose, when feasible (48).

For RTX, the panel recommended to time RTX administration (of the next/first dose, if given as part of a multidose cycle) 2–4 weeks after the second vaccine dose, if possible, but added the condition that the patient’s disease should be under acceptable control to allow this delay, especially given the extended gap (e.g., 6 months) between RTX cycles (65,80–82). The task force acknowledged that the evidence base supporting the recommendations related to RTX timing was largely based on studies of humoral immunity following receipt of other vaccines (60–63,65,70,80–83), which had uncertain generalizability to vaccination against COVID-19, especially since the degree to which efficacy is attributable to induction of host T cell versus B cell (antibody-based) immunity is uncertain at this time.

As an outgrowth of the evidence report, the task force assembled a research agenda where evidence was lacking (Table 6). Given that there was little direct evidence in any RMD population, the topics were broad and spanned domains related to clinical effectiveness, safety, flare, reactogenicity, study design, immunogenicity, and laboratory-based correlates of protection. With the relatively small size of the task force, no attempt was made to prioritize these topics given the expectation that they would evolve over time and as new science in non-RMD populations was forthcoming.

**DISCUSSION**

This ACR guidance encompasses the optimal use of COVID-19 vaccines for patients with rheumatic and musculoskeletal diseases. It is intended to aid in the care of individual patients but not to supplant personalized care or constrain shared decision-making with patients. The mRNA vaccine platform is novel, and considerations for vaccines developed on this platform may differ from those relevant to other vaccines. The guidance regarding the use and timing of immunomodulatory medications was based on extrapolation of the available evidence of their immunologic effects as they relate to other vaccines and vaccine platforms. As such, all of these recommendations are considered conditional. Finally, the task force advised health care providers to avoid being overly dogmatic in following these recommendations. The attempt to optimize vaccine response in relation to the use and timing of immunosuppressive medications should not compromise a willing patient’s ability to undergo vaccination in a timely manner and risk a missed vaccination opportunity.

As an overarching principle, the sparsity of information regarding COVID-19 vaccination in RMD patients and lack of direct evidence yielded a need for extrapolation based on the literature published for other vaccines. The evidence base was, therefore, of low or very low quality and suffered from indirectness (12) in almost all respects. The guidance provided herein

---

**Table 6.** Research agenda for future COVID-19 vaccine studies in RMD patients proposed by the task force*

| Research Agenda Area                                                                 | Examples                                                                 |
|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Conduct clinical efficacy and laboratory-based immunogenicity studies in RMD patients following vaccination, especially for AIIRD patients receiving certain immunomodulatory therapies (e.g., methotrexate, abatacept, JAK inhibitors, rituximab, GCs). | Optimize vaccine response by considering timing related to intentional short-term cessation of certain immunomodulatory therapies (e.g., methotrexate, subcutaneous abatacept, JAK inhibitors) to optimize vaccine response. |
| Evaluate risk of disease flare, disease worsening, and systemic reactivity following COVID-19 vaccination in RMD patients, by disease and in relation to background immunomodulatory therapies. | Directly compare vaccines and vaccine platforms for the above efficacy, immunogenicity, and safety outcomes: notable given the potential for some COVID-19 vaccines to achieve the minimum threshold for the FDA’s EUA yet have seemingly lower vaccine efficacy based on large clinical trials in non-RMD patients. |
| Long-term follow-up for durability and magnitude of vaccine protection in relation to various immunomodulatory medications, and as new SARS-CoV-2 strains emerge. | Long-term follow-up for durability and magnitude of vaccine protection in relation to various immunomodulatory medications, and as new SARS-CoV-2 strains emerge. |
| Assess benefits and timing of additional COVID-19 vaccine administration (i.e., booster dose). | Assess benefits and timing of additional COVID-19 vaccine administration (i.e., booster dose). |
| Generate real-world evidence (e.g., large pragmatic trial or observational studies) embedded in routine clinical practice to study the above topics, especially to promote large-scale safety surveillance. | Generate real-world evidence (e.g., large pragmatic trial or observational studies) embedded in routine clinical practice to study the above topics, especially to promote large-scale safety surveillance. |
| Establish a biorepository with associated clinical data infrastructure to facilitate future COVID-19 (and possibly other) vaccine-related research in RMD patients, considering the future potential to identify laboratory-based correlates of protection relevant for individual patients. | Identify laboratory-based serologic testing to identify patients with a suboptimal response to COVID-19 vaccination who might be candidates for a booster dose or need to repeat the vaccination series. |
| Identify COVID-19 vaccine–induced immune parameters (immunogen-specific neutralizing antibody levels, total immunogen-specific antibody levels or isotypes, T cell immunity, innate immunity) or host determinants that are predictive of successful host response to vaccine, as reflected by protection from infection or mitigation of morbidity during subsequent infection. | Identify COVID-19 vaccine–induced immune parameters (immunogen-specific neutralizing antibody levels, total immunogen-specific antibody levels or isotypes, T cell immunity, innate immunity) or host determinants that are predictive of successful host response to vaccine, as reflected by protection from infection or mitigation of morbidity during subsequent infection. |
| Conduct large epidemiology studies of COVID-19 outcomes (e.g., using large administrative databases of health plans, electronic health record data [e.g., the ACR RISE registry], or other data sources or methods) and examine the role of AIIRD disease features, treatments, and vaccination. While risk factors for incident disease may be shaped by confounding and unmeasured variability in exposure, examining outcomes conditioning on incident COVID-19 diagnosis may be more fruitful. | Conduct large epidemiology studies of COVID-19 outcomes (e.g., using large administrative databases of health plans, electronic health record data [e.g., the ACR RISE registry], or other data sources or methods) and examine the role of AIIRD disease features, treatments, and vaccination. While risk factors for incident disease may be shaped by confounding and unmeasured variability in exposure, examining outcomes conditioning on incident COVID-19 diagnosis may be more fruitful. |

---

* COVID-19 = coronavirus disease 2019; RMD = rheumatic and musculoskeletal disease; AIIRD = autoimmune and inflammatory rheumatic disease; GCs = glucocorticoids; FDA = US Food and Drug Administration; EUA = Emergency Use Authorization; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; ACR = American College of Rheumatology; RISE = Rheumatology Informatics System for Effectiveness.
represents a balance between evidence regarding efficacy, effectiveness, safety, feasibility (e.g., withholding a therapy with a long half-life or extended recirculation like leflunomide may be unrealistic), expected vaccine availability, and tradeoffs in resource utilization. For example, vigorous debate was held about whether it was preferable to vaccinate a high-risk patient in a suboptimal circumstance (e.g., active disease, receiving high-dose glucocorticoids, receiving cytotoxic therapy), under the assumption that the vaccine would confer at least some protection to a patient at high risk for a poor outcome if they contract COVID-19. Or rather, might it be preferable to wait until a more optimal circumstance presented itself? However, given the uncertainty in most medical settings to predict the future course of a patient’s AIIRD or the need for additional immunomodulatory treatments, a more salutary setting to optimize vaccine response might never materialize. Thus, the task force typically favored proceeding more immediately with vaccination.

If a laboratory-based correlate of protection existed that could serve as a proxy for immunity, and if a booster dose could be administered or the vaccine series repeated at a later time, there would be greater certainty to recommend vaccinating all patients immediately, regardless of setting or underlying treatment. These societal considerations regarding vaccine allocation in light of constrained vaccine supply and regional resource limitations to vaccinate posed important tradeoffs for the panel. Given tradeoffs like these, the extant uncertainties posed by the scoping questions informed by imperfect evidence, and the highly dynamic environment of vaccination implementation, the task force recommended as it did.

The strengths of this effort are notable given the urgent need presented by the availability of new COVID-19 vaccines and critical questions about how to best use those vaccines for RMD patients. The task force generated an evidence summary over a very compressed time frame and leveraged a well-established consensus methodology process used previously by the ACR. Of high importance, the task force’s composition included experts in rheumatology, infectious disease, and public health, representing a plurality of different stakeholder perspectives.

Regarding important limitations, our ability to generalize from the literature for other vaccines and vaccine platforms in RMD patients to the novel COVID-19 vaccines now available in the US is limited. Vaccination against SARS-CoV-2 raises different issues than those for other vaccine-preventable illnesses, given the potential for ongoing public health measures to partially mitigate exposure. This guidance therefore must be interpreted by clinicians and patients in light of underlying principles rather than considering them either prescriptive or proscriptive. For example, an AIIRD patient with minimal public contact who is able to strongly adhere to all preventive health measures might choose to withhold RMD treatments or briefly defer vaccination in accordance with this guidance, whereas this same decision may not be possible for a patient employed in a high-risk setting (e.g., front-line health care, or long-term care facility). From a vaccine policy and recommendation context, the task force prioritized simplicity, noting that this guidance would be expected to apply to the care of most RMD patients in most settings.

Finally, the procedures used to develop this guidance did not follow the rigorous methodology routinely used by the ACR when formal clinical practice guidelines are created, although they were adherent to the ACR standardized operating procedures for guidance documents (13). This was an expected limitation given the accelerated time frame desired by the ACR to issue practical and timely recommendations both to its membership and to the rheumatology community. Once the urgency of the pandemic has passed, the work of this task force will eventually be folded back under the aegis of the broader ACR Vaccine Guideline development group, charged with covering this and all other vaccines in the context of RMDs, and the more typical guideline development process favored by the ACR will be applied. Additional and important input from other stakeholders, including patients and patient advocates will also be sought, as the ACR has done for past clinical practice guidelines (6).

As new safety and efficacy evidence becomes available for both mRNA vaccines and other vaccine platforms in patients with RMDs and AIIRDs, the ACR’s guidance document will continue to be updated and expanded, consistent with the notion of a “living document.” The ACR is committed to maintaining this process throughout the pandemic to facilitate evidence-based practice and promote optimal outcomes for all patients with RMDs and AIIRDs with respect to mitigating COVID-19 risk.

ACKNOWLEDGMENTS

The task force would like to thank Dr. Kenneth Saag (UAB) for his initial review of the draft rating statements, Kaitlin Nichols (UAB) for her assistance in manuscript development, and Regina Parker (ACR) for her role in coordinating the activities of the Task Force.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Curtis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Sadun, Turner, Williams, Mikuls.

Acquisition of data. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Sadun, Turner, Williams, Mikuls.

Analysis and interpretation of data. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Sadun, Turner, Williams, Mikuls.

REFERENCES

1. Van der Heijde D, Daikh DI, Betteridge N, Burmester GR, Hassett AL, Matteson EL, et al. Common language description of the term rheumatic and musculoskeletal diseases (RMDs) for use
in communication with the lay public, healthcare providers, and other stakeholders endorsed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR). Arthritis Rheumatol 2018;70:826–31.

2. Mikuls TR, Johnson SR, Fraenkel L, Arasaratnam RJ, Baden LR, Bermas BL, et al. American College of Rheumatology guidance for the management of rheumatic disease in adult patients during the COVID-19 pandemic: version 3. Arthritis Rheumatol 2021;73:e1–12.

3. US Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee meeting: FDA briefing document Pfizer-BioNTech COVID-19 vaccine. December 2020. URL: https://www.fda.gov/media/144245/download.

4. US Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee meeting: FDA briefing document Moderna COVID-19 vaccine. December 2020. URL: https://www.fda.gov/media/144434/download.

5. Singh JA, Kurz DE, Bharat A, Curtis JR, Kavanaugh AF, Herzenberg LA, et al. 2018 update of the American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken) 2012;64:625–39.

6. Singh JA, Saag KG, Bridges SL Jr, Altdorfer W, Sullivan MC, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol 2016;68:1–26.

7. Fraenkel L, Batthom JM, England BR, St.Clair EW, Arayessi T, Carandang K, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol 2021 doi: http://onlinelibrary.wiley.com/doi/10.1002/art.41752/abstract. E-pub ahead of print.

8. Singh JA, Guyatt G, Ogdie A, Gladman DD, Dale C, Dodchan A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation guideline for the treatment of psoriatic arthritis. Arthritis Rheumatol 2019;71:5–32.

9. Furer V, Rondaan C, Heijstek MW, Agmon-Levin N, van Assen S, Bijl M, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2020;79:39–52.

10. Rondaan C, Furer V, Heijstek MW, Agmon-Levin N, Bijl M, Breedveld FC, et al. Efficacy, immunogenicity and safety of vaccination in adult patients with autoimmune inflammatory rheumatic diseases: a systematic literature review for the 2019 update of EULAR recommendations. RMD Open 2019;5:e001035.

11. Van Assen S, Agmon-Levin N, Elkayam O, Cervera R, Doran MF, Dougdas M, et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2011;70:414–22.

12. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 8. Rating the quality of evidence-‐indirectness. J Clin Epidemiol 2011;64:1303–10.

13. American College of Rheumatology. American College of Rheumatology Guidance Subcommittee and Endorsement of Guidance Documents, 2020. URL: https://www.rheumatology.org/Portals/0/Files/ACR-Guidance-Subcommittee-Procedures-FrameWork.pdf.

14. Fitch K, Bernstein SJ, Aguilar MD, Bunnard B, LaCelle JR, Lazzaro P, et al. The RAND/UCLAappropriateness method user’s manual. Santa Monica (CA): RAND; 2001.

15. American College of Rheumatology. COVID-19 guidance. URL: https://www.rheumatology.org/Practice-Quality/Classic-Support/COVID-19-Guidance.

16. ModernaTX, sponsor. A study to evaluate the safety, reactogenicity, and effectiveness of mRNA-1273 vaccine in adolescents 12 to <18 years old to prevent COVID-19 (TeenCove). ClinicalTrials.gov identifier: NCT04649151.

17. BioNTech SE and Pfizer, sponsors. Study to describe the safety, tolerability, immunogenicity, and efficacy of mRNA vaccine candidates against COVID-19 in healthy individuals. ClinicalTrials.gov identifier: NCT04366728.

18. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:e44–100.

19. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309–18.

20. Blumentals WA, Arreglado A, Napalkov P, Toohey S. Rheumatoid arthritis and the incidence of influenza and influenza-related complications: a retrospective cohort study. BMC Musculoskelet Disord 2012;13:158.

21. Van Assen S, Elkayam O, Agmon-Levin N, Cervera R, Doran MF, Dougdas M, et al. Vaccination in adult patients with auto-immune inflammatory rheumatic diseases: a systematic literature review for the European League Against Rheumatism evidence-based recommendations for vaccination in adult patients with auto-immune inflammatory rheumatic diseases [review]. Autoimmun Rev 2011;10:341–62.

22. Yun H, Yang S, Chen L, Xie F, Winthrop K, Baddley JW, et al. Risk of herpes zoster in autoimmune and inflammatory diseases: implications for vaccination. Arthritis Rheumatol 2016;68:2232–37.

23. Cordtz R, Lindhardsen B, Souccsi BD, Vela J, Uhrenholdt L, Westermann R, et al. Incidence and severity of COVID-19 hospitalisation in patients with inflammatory rheumatic disease: a nationwide cohort study from Denmark. Rheumatology (Oxford) 2020. E-pub ahead of print.

24. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430–6.

25. D’Silva KM, Jorge A, Cohen A, McCormick N, Zhang Y, Wallace ZS, et al. COVID-19 outcomes in patients with systemic autoimmune rheumatic diseases compared to the general population: a US multicenter, comparative cohort study. Arthritis Rheumatol 2021;73:914–20.

26. Topless R, Phipps-Green A, Leask M, Dalbeth N, Luk S, Robinson P, et al. Gout, rheumatoid arthritis and the risk of death from COVID-19: an analysis of the UK Biobank. medRxiv 2021. E-pub ahead of print.

27. Eder L, Croxford R, Drucker A, Mendel A, Kuriya B, Touma Z, et al. COVID-19 hospitalizations, ICU admission, and death among Ontario residents with immune mediated inflammatory diseases. J Rheumatol 2021. E-pub ahead of print.

28. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.

29. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934–43.

30. Gianfrancesco MA, Leykina LA, Izadi Z, Taylor T, Sparks JA, Harrison C, et al. Association of race and ethnicity with COVID-19 outcomes in rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Arthritis Rheumatol 2021;73:574–80.

31. Strangfeld A, Schäfer M, Gianfrancesco MA, Lawson-Tovey S, Liew WC, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2021. E-pub ahead of print.

32. Gianfrancesco M, Hyrich KL, Al-Adey S, Carmona L, Danila MI, Gossel L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the
COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2020;79:859–66.

33. Ungaro RC, Agrawal M, Park S, Hirtre R, Colombel JF, Twyman K, et al. Autoimmune and chronic inflammatory disease patients with COVID-19. ACR Open Rheumatol 2021;3:111–5.

34. Choi B, Choudhary MC, Regan J, Sparks JA, Padera RF, Qiu X, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host [letter]. N Engl J Med 2020;383:2291–3.

35. Centers for Disease Control and Prevention. Vaccine recommendations and guidelines of the ACIP: COVID-19 vaccine recommendations. March 2021. URL: https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html.

36. Centers for Disease Control and Prevention. Vaccines and immunizations: interim considerations—preparing for the potential management of anaphylaxis after COVID-19. Vaccination. March 2021. URL: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fpflizer%2Fanaphylaxis-management.html.

37. Yun H, Xie F, Baddley JW, Winthrop K, Saag KG, Curtis JR. Long-term effectiveness of herpes zoster vaccine among patients with autoimmune and inflammatory diseases. J Rheumatol 2017;44:1083–7.

38. Park JK, Lee YJ, Shin K, Ha YJ, Lee EY, Song YW, et al. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis 2018;77:898–904.

39. Van der Maas A, Lie E, Christensen R, Choy E, de Man YA, van Riel PLM. Effect of methotrexate discontinuation on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a post-hoc analysis of two randomised trials. Clin Rheumatol 2020;39:375–9.

40. Park JK, Kim MJ, Choi Y, Winthrop K, Song YW, Lee EB. Effect of short-term methotrexate discontinuation on rheumatoid arthritis disease activity: post-hoc analysis of two randomized trials. Clin Rheumatol 2020;39:375–9.

41. Park JK, Choi Y, Winthrop KL, Song YW, Lee EB. Optimal time between the last methotrexate administration and seasonal influenza vaccination in rheumatoid arthritis: post hoc analysis of a randomised clinical trial [letter]. Ann Rheum Dis 2019;78:1283–4.

42. Park JK, Lee MA, Lee EY, Song YW, Choi Y, Winthrop KL, et al. Effect of methotrexate discontinuation on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis 2017;76:1559–65.

43. Oda R, Inagaki T, Ishikane M, Hotta M, Shimomura A, Sato M, et al. Case of adult large vessel vasculitis after SARS-CoV-2 infection [Letter]. Ann Rheum Dis 2020. E-pub ahead of print.

44. Perrot L, Hemon M, Busnel JM, Muis-Pistor O, Picard C, Zandotti M, et al. First flare of ACPA-positive rheumatoid arthritis after SARS-CoV-2 infection. Lancet Rheumatol 2021;3:e6–8.

45. Baden LR, Walsh SR, Seaman MS, Tucker RP, Krause KH, Patel A, et al. First-in-human evaluation of the safety and immunogenicity of a recombinant adenovirus serotype 26 H1N1 Env vaccine [IPCAVD 001]. J Infect Dis 2013;207:240–7.

46. Centers for Disease Control and Prevention. Vaccines and immunizations: interim clinical considerations for use of mRNA COVID-19 vaccines currently authorized in the United States. March 2021. URL: https://www.cdc.gov/vaccines/covid-19/info-by-product/mRNA.html.

47. Elkayam O, Amir S, Mendelson E, Schwaber M, Grotto I, Wollman J, et al. Efficacy and safety of vaccination against pandemic 2009 influenza A (H1N1) virus among patients with rheumatic diseases. Arthritis Care Res (Hoboken) 2011;63:1062–7.

48. Battafarano DF, Battafarano NJ, Larsen L, Dyer PD, Older SA, Muehlbauer S, et al. Antigen-specific antibody responses in lupus patients following immunization. Arthritis Rheum 1998;41:1828–34.

49. Mok CC, Ho LY, Fong LS, To CH. Immunogenicity and safety of a quadrivalent human papillomavirus vaccine in patients with systemic lupus erythematosus: a case–control study. Ann Rheum Dis 2013;72:659–64.

50. Bingham CO III, Rizzo W, Kivitz A, Hassanali A, Upmanyu R, Klearman M. Humoral immune response to vaccines in patients with rheumatoid arthritis treated with tocilizumab: results of a randomised controlled trial (VISARA). Ann Rheum Dis 2015;74:818–22.

51. Mori S, Ueki Y, Akeda Y, Hirakata N, Oribe M, Shiohira Y, et al. Pneumococcal polysaccharide vaccination in rheumatoid arthritis patients receiving tocilizumab therapy. Ann Rheum Dis 2013;72:1362–6.

52. Mori S, Ueki Y, Hirakata N, Oribe M, Hidaka T, Oishi K. Impact of tocilizumab therapy on antibody response to influenza vaccine in patients with rheumatoid arthritis. Ann Rheum Dis 2012;71:2006–10.

53. Sahin U, Mulk A, Derhovanessian E, Vogler I, Kranz LM, Vormehr M, et al. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses. Nature 2020;586:594–9.

54. Tsuru T, Terao K, Murakami M, Matsutani T, Suzaki M, Amamoto T, et al. Immune response to influenza vaccine and pneumococcal polysaccharide vaccine under IL-6 signal inhibition therapy with tocilizumab. Mod Rheumatol 2014;24:511–6.

55. Migita K, Akeda Y, Akazawa M, Tohma S, Hirano F, Ideguchi H, et al. Pneumococcal polysaccharide vaccination in rheumatoid arthritis patients receiving tacrolimus. Arthritis Res Ther 2015;17:149.

56. Doornekamp L, Goetgebuer RL, Schmitz KS, Goeminne M, van der Woude CJ, Foucher R, et al. High immunogenicity to influenza vaccination in Crohn’s disease patients treated with ustekinumab. Vaccines (Basel) 2020;8:455.

57. Furer V, Rondalla C, Heijstek M, van Asssen S, Blij M, Agmon-Levin N, et al. Incidence and prevalence of vaccine preventable infections in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD): a systemic literature review informing the 2019 update of the EULAR recommendations for vaccination in adult patients with AIIRD. RMD Open 2019;5:e001041.

58. Furer V, Zisman D, Kaufman I, Arad U, Berman M, Sarbagli-Maman H, et al. Immunogenicity and safety of vaccination against seasonal influenza vaccine in patients with psoriatic arthritis treated with secukinumab. Vaccine 2020;38:847–51.

59. Richi P, Martin MD, de Ory F, Gutiérrez-Lamaya R, Casas I, Jiménez-Díaz AM, et al. Secukinumab does not impair the immunogenic response to the influenza vaccine in patients. RMD Open 2019;5:e001018.

60. Bar-Or A, Calkwood JC, Chognot C, Evershed J, Fox EJ, Herman A, et al. Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: the VELOCE study. Neurology 2020;95:e1999–2008.

61. Nazi I, Kelton JG, Larche M, Snider DP, Heddie NM, Crowther MA, et al. The effect of rituximab on vaccine responses in patients with autoimmune inflammatory rheumatic diseases (AIIRD). A systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2014;66:1016–26.

62. Houot R, Levy R, Cartron G, Armand P. Could anti-CD20 therapy jeopardise the efficacy of a SARS-CoV-2 vaccine? Eur J Cancer 2020;136:4–6.

63. Bar-Or A, Calkwood JC, Chognot C, Evershed J, Fox EJ, Herman A, et al. Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: the VELOCE study. Neurology 2020;95:e1999–2008.

64. Hua C, Barnetche T, Combe B, Morel J. Effect of methotrexate, anti-tumor necrosis factor α, and rituximab on the immune response to influenza and pneumococcal vaccines in patients with rheumatoid arthritis: a systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2014;66:1016–26.

65. Van Assen S, Holvast A, Benne CA, Posthumus MA, van Leeuwen MA, Voskuyl AE, et al. Humoral responses after influenza vaccination are severely reduced in patients with rheumatoid arthritis treated with rituximab. Arthritis Rheum 2010;62:75–81.
66. Aikawa NE, Campos LM, Silva CA, Carvalho JF, Saad CG, Trudes G, et al. Glucocorticoid: major factor for reduced immunogenicity of 2009 influenza A (H1N1) vaccine in patients with juvenile autoimmune rheumatic disease. J Rheumatol 2012;39:167–73.

67. Kim EY, Lim JE, Jung JY, Son JY, Lee KJ, Yoon YW, et al. Performance of the tuberculin skin test and interferon-γ release assay for detection of tuberculosis infection in immunocompromised patients in a BCG-vaccinated population. BMC Infect Dis 2009;9:207.

68. Nagel J, Saxne T, Geborek P, Bengtsson AA, Jacobsen S, Joergensen CS, et al. Treatment with belimumab in systemic lupus erythematosus does not impair antibody response to 13-valent pneumococcal conjugate vaccine. Lupus 2017;26:1072–81.

69. Subesinghe S, Bechman K, Rutherford AI, Goldblatt D, Galloway JB. A systematic review and metaanalysis of antirheumatic drugs and vaccine immunogenicity in rheumatoid arthritis. J Rheumatol 2018;45:733–44.

70. Adler S, Krivine A, Weix J, Rozenberg F, Launay O, Huesler J, et al. Protective effect of A/H1N1 vaccination in immune-mediated disease—a prospectively controlled vaccination study. Rheumatology (Oxford) 2011;51:695–700.

71. Ribeiro AC, Laurindo IM, Guedes LK, Saad CG, Moraes JC, Silva CA, et al. Abatacept and reduced immune response to pandemic 2009 influenza A/H1N1 vaccination in patients with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2013;65:476–80.

72. Kapetanovic MC, Nagel J, Nordstrom I, Saxne T, Geborek P, Rudin A. Methotrexate reduces vaccine-specific immunoglobulin levels but not numbers of circulating antibody-producing B cells in rheumatoid arthritis after vaccination with a conjugate pneumococcal vaccine. Vaccine 2017;35:903–9.

73. Kapetanovic MC, Roseman C, Jönsson G, Truedsson L, Saxne T, Geborek P. Antibody response is reduced following vaccination with 7-valent conjugate pneumococcal vaccine in adult methotrexate-treated patients with established arthritis, but not those treated with tumor necrosis factor inhibitors. Arthritis Rheum 2011;63:3723–32.

74. Winthrop KL, Silverfield J, Racewicz A, Neal J, Lee EB, Hrycaj P, et al. The effect of tofacitinib on pneumococcal and influenza vaccine responses in rheumatoid arthritis. Ann Rheum Dis 2016;75:687–95.

75. Winthrop KL, Bingham CO III, Komocsar WJ, Bradley J, Issa M, Klar R, et al. Evaluation of pneumococcal and tetanus vaccine responses in patients with rheumatoid arthritis receiving baricitinib: results from a long-term extension trial substudy. Arthritis Res Ther 2019;21:102.

76. Gabraith MD, Kinning KT, Sullivan KD, Baxter R, Araya P, Jordan KR, et al. Serocconversion stages COVID19 into distinct pathophysiological states. medRxiv 2020. E-pub ahead of print.

77. Alten R, Bingham CO III, Cohen SB, Curtis JR, Kelly S, Wong D, et al. Antibody response to pneumococcal and influenza vaccination in patients with rheumatoid arthritis receiving abatacept. BMC Musculoskelet Disord 2016;17:231.

78. Kapetanovic MC, Kristensen LE, Saxne T, Aktas T, Mörner A, Geborek P. Impact of anti-rheumatic treatment on immunogenicity of pandemic H1N1 influenza vaccine in patients with arthritis. Arthritis Res Ther 2014;16:R2.

79. Migita K, Akeda Y, Akazawa M, Tohma S, Hirano F, Ideguchi H, et al. Effect of abatacept on the immunogenicity of 23-valent pneumococcal polysaccharide vaccination (PPSV23) in rheumatoid arthritis patients. Arthritis Res Ther 2015;17:357.

80. Bingham CO III, Looney RJ, Deodhar A, Halsey N, Greenwald M, Codding C, et al. Immunization responses in rheumatoid arthritis patients treated with rituximab: results from a controlled clinical trial. Arthritis Rheum 2010;62:64–74.

81. Westra J, van Assen S, Wilting KR, Land J, Horst G, de Haan A, et al. Rituximab impairs immunoglobulin (IgM and IgG subclass) responses after influenza vaccination in rheumatoid arthritis patients. Clin Exp Immunol 2014;178:40–7.

82. Rehnberg M, Brissielt M, Amu S, Zendjanchi K, Häwi G, Bokarewa M. Vaccination response to protein and carbohydrate antigens in patients with rheumatoid arthritis after rituximab treatment. Arthritis Res Ther 2010;12:R111.

83. Arad U, Tzadok S, Amir S, Mandelboim M, Mendelson E, Wigler I, et al. The cellular immune response to influenza vaccination is preserved in rheumatoid arthritis patients treated with rituximab. Vaccine 2011;29:1643–8.