American College of Rheumatology (ACR)
Updated Guideline for the Management of Rheumatoid Arthritis

Public Comments

The ACR Updated Guideline for the Management of Rheumatoid Arthritis public comment was posted on the ACR website October 30, 2018. The announcement was e-mailed to the Practice Guidelines Subcommittee, Quality of Care Committee and ACR Board of Directors, and was included in multiple ACR publications and on ACR social media platforms. ***Five (5)*** *responses were received via the online form and* ***one (1)*** *was sent via email. The public comment period closed on November 30, 2018.*

RESPONSES RECEIVED ONLINE:

- **Name:** Veronica De Cillis
- **Institution:** Hospital Manuel Rocca (Argentina)
- **Position:** Occupational Therapy
- **Disclosure (optional):** Nothing to disclose

Comment:

- 528 p17. Patients should use standardized self-management program because it helps them with arthritis self-efficacy, pain, fatigue and to prevent treatment-related harms.
- 553 p18. Patients should use splinting/orthoses to relieve pain, prevent deformity and improve/ maintenance function in a long term.
- 556 p 18. Patients should do hand exercises depending on disease activity
- 573 p19. Patients should use joint protection techniques in order to relieve pain, prevent deformity and improve/maintenance function in a long term.
- 586 p19. Patients who would like to be employed or those who are should use work interventions so "Arthritis does not affect their work and their work does not affect their arthritis."
- 593 p19. Patients should participate in comprehensive occupational therapy in order to learn arthritis self-efficacy, treatment-related harms and objective measure of function.

- **Name:** Corey Greenblatt
- **Institution:** Global Healthy Living Foundation
- **Position:** Manager, Policy and Advocacy
- **Disclosure (optional):** Nothing to disclose

Comment:
The Global Healthy Living Foundation (GHLF) appreciates the opportunity to provide comments on the Rheumatoid Arthritis Guideline Project Plan. GHLF is a 20-year-old 501(c)(3) patient advocacy organization representing chronically ill patients and their caregivers across the country. We work to improve the quality of life for patients living with chronic disease by making sure their voices are heard and advocating for improved access to care at the community level. Our patients are suffering from chronic conditions that are often accompanied by chronic pain, including arthritis, psoriasis, cardiovascular disease and migraine. We are pleased to see that the American College of Rheumatology (ACR) is honoring its commitment to patients by providing a public comment period for the updated Rheumatoid Arthritis Guideline Project Plan.

GHLF aligns with ACR over the need for consensus and standardization of treatment in healthcare and thus we understand the importance of these guidelines. At the same time, on behalf of patients, we also

voice the need for personalized treatment so that patients and clinicians can achieve their shared goals. This is especially true in order for treat-to-target to be effective. One area that we are glad to see ACR including in the updated guidelines in some guidance about vaccinations. This is an area of immense concern for many patients with RA and there is currently a lot of inconsistency in terms of what patients are advised to do. An area that GHLF would request ACR to look further into including is guidance over the management of over-the-counter medications such as NSAIDS, which remains a concern for our patient community. Additionally, GHLF supports the fact that these recommendations are a result of multistakeholder conversations and discussions which have included the voices and concerns of patients.

Again, we commend ACR for upholding their commitment to patients and look forward to continuing to serve as a resource. If you have any questions, please contact Louis Tharp (ltharp@ghlf.org), 845-323-8408, co-founder and Executive Director.

- **Name:** Janet Poole
- **Institution:** University of New Mexico
- **Position:** Director, Occupational Therapy Graduate Program
- **Disclosure (optional):** I am the president-elect of ARP.

Comment:
Starting on page 16, questions 33 - 51 regarding DMARDs and non-pharmacological therapies, many articles on community-based programs may not collect information on DMARDs or levels of disease activity. Will these studies be excluded? I hope not.

Regarding grading the "quality" of evidence, there are those who argue that quality of rehabilitation and behavioral/activity-type interventions cannot be evaluated the same way as pharmacological studies (see for example Johnston, Sherer, Whyte, Am J Phy Med Rehabil, 2006, 85: 292-309; Gerber et al. Disability & Health J, 2016; 9, 559-566.). Thus, often non-pharmacological are not included in recommended guidelines.

- **Name:** Sheila Kelly
- **Institution:** Bristol-Myers Squibb
- **Position:** Immunoscience Group Director, US Medical
- **Disclosure (optional):** This response was provided by the medical and scientific content departments at Bristol-Myers Squibb.

Comment:
On behalf of Bristol-Myers Squibb, please find our response to the American College of Rheumatology (ACR) call for public comment on the draft Project Plan to update the 2015 ACR Guideline for the Treatment of Rheumatoid Arthritis. As requested, we have submitted our response electronically via the portal located on ACR's website.

Please note that Bristol-Myers Squibb does not recommend the use of a product in any manner inconsistent with that described in the ORENCIA full Prescribing Information (https://packageinserts.bms.com/pi/pi_orencia.pdf).

Public Comments

If you have further questions or require additional information, please contact Sheila Kelly, MD Bristol-Myers Squibb, Group Director Immunoscience; phone: 609-302-4999; sheila.kelly@bms.com. Thank you for the opportunity to provide comments on the ACR Project Plan.

Line Number	Comment
13, 18-21	The ACR guidelines previously provided a list of poor prognostic factors (PPFs) that included rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, extra-articular disease, etc.[1] The EULAR guidelines continues to provide a similar list of PPFs that includes many of the same factors, such as RF and anti-CCP.[2] BMS suggests that PPFs be added again to this next update of the guidelines.
20	The ACR mentions interstitial lung disease (ILD). BMS would like to suggest the ACR consider treatment specific guidance for patients with ILD in the literature search.
22	The ACR mentions atherosclerotic plaques and cardiovascular diseases. Large real world study suggests there may be class differences.[3] BMS suggests that a guideline-specific question be added. Certain datasets show especially poor outcomes for RA patients with diabetes[3] or CV disease.[4,5] BMS suggests patients with diabetes or cardiovascular (CV) disease have distinct consideration in the ACR guidelines literature searches.
47	BMS suggests adding diabetes and cardiovascular disease as comorbidities requiring specific treatment guidance.
263	In addition to risk factors, subpopulations vary based on safety, and on biomarkers/serology and other poor prognostic factors. These differences may predict a different response or experience by treatment class. BMS suggests that these additional factors also be taken into consideration when developing recommendations.
318-323	BMS supports re-assessing the interval for treatment escalation.
340-349	BMS suggests adding a similar statement to the one in lines 665 and 673 *(Recommendations may differ for subpopulations with varying risk factors)*, but also include ACPA status, and other poor prognostic factors.
415 and 425	• BMS suggests that a search of all literature be conducted looking at mechanism of action (MOA) switch vs. cycling agents with the same MOA. • BMS supports assessing whether a new MOA is warranted in patients who are not at target or who have primary failure. • BBM suggests also adding a similar statement to the one in lines 665 and 673 *(Recommendations may differ for subpopulations with varying risk factors)*, but also include ACPA status, and other poor prognostic factors; and to consider these in their literature search.
665 and 673	BMS suggests revising the statement in these 2 lines to read: ***Recommendations may differ for subpopulations with varying risk factors and poor prognostic factors (e.g., the biomarkers such as anti-cpp2 seropositivity).*** ACR discussed poor prognostic factors in the previous 2008 and 2012 guidelines, but not in the most recent 2015 guidelines. Since then studies have been conducted, real-world and clinical[6,7,8], that may inform treatment choice for patient with poor prognostic factors, such as positive autoantibody status. BMS suggests specific recommendations are given for patients with seropositive RA.
634	Studies such as the RETRO study suggest that patients in remission and those with anti-CCP antibodies seroconversion or low MBDA (serological remission) maintain remission significantly longer than patients in clinical remission that are not in serological remission.[9] BMS suggests that ACR consider in their literature search "serologic remission."

659	BMS suggests that ACR searches for dose reduction for patients in remission and that ACR consider search terms like "serologic remission" and "immunologic remission" when considering tapering strategies.
673	BMS suggests including sub-population monitoring, monitoring imaging and serology (antibodies, CRP, other inflammatory surrogates).
691	BMS suggests that dose reductions of IV products be considered in the literature search.
752-753	Wunderlich et al. has data suggesting total IgG reductions do not occur with all adaptive immune inhibiting drugs.[8]
766, 779	Please consider other country-level guidelines and approach in providing therapeutic recommendations for these questions.
917, 926	Suggest referring to NCCN guidelines for alignment. Sections of interest: treatment, monitoring and concomitant medications.

References:

1. Singh, et al. 2012 update of the 2008 American College of Rheumatology (ACR) Recommendations for the use of disease-modifying anti-rheumatic drugs and biologics in the treatment of rheumatoid arthritis (RA). Arthritis Care Res (Hoboken). 2012; 64(5): 625–639.
2. Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017;0:1–18. doi:10.1136/annrheumdis-2016-210715
3. Kang EH, et al. Comparative cardiovascular risk of abatacept and tumor necrosis factor inhibitors in patients with rheumatoid arthritis with and without diabetes mellitus: A multidatabase cohort study. J Am Heart Assoc. 2018;7(3).
4. Dougados M, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis. 2014;73:62-68.
5. Lopez-Longo FJ, et al. Association between anti-cyclic citrullinated peptide antibodies and ischemic heart disease in patients with rheumatoid arthritis. Arthritis Rheum. 2009;61:419-424.
6. Harrold LR et al. J Rheumatol 2018:45:32-39.
7. Sokolove J et al. Ann Rheum Dis 2016;75:709–714.
8. Wunderlich C,et al. Effects of DMARDs on citrullinated peptide autoantibody levels in RA patients—A longitudinal analysis. Sem Arthritis Rheumatism. 2017; 46: 709–714
9. Figueiredo CP, et al. Antimodified protein antibody response pattern influences the risk for disease relapse in patients with rheumatoid arthritis tapering disease modifying antirheumatic drugs. Ann Rheum Dis. 2017;76:399–407.

- **Name:** Pat Allen
- **Institution:** Learning Innovations, Inc.
- **Position:** President
- **Disclosure (optional):** Nothing to disclose.

Comment:

Please consider that "patient needs come first" as the Mayo team promotes. That includes focusing on meeting the learning needs of patients, doctors and other service providers by understanding learning preferences of individuals in team learning situations.

RESPONSE RECEIVED VIA EMAIL:

- **Name:** V. Michael Holers

- **Institution:** University of Colorado
- **Position:** Professor, Molecular Biology
- **Disclosure (optional):** I am a member of the ACR Board of Directors.

Comment:

My only thought regarding the rheumatoid arthritis guidelines is for the group to consider taking on the approach to individuals who are stably anti-CCP+ without inflammatory arthritis, and with or without arthralgia (the so-called Clinically Suspect Arthralgia) and/or ultrasound findings. This is a major area of emphasis within the EULAR efforts on RA prevention and induction of tolerance, and is something we are increasingly hearing about as a clinical issue in the U.S., relative to Kevin Deane's NIH-funded StopRA clinical prevention trial. I would be happy to discuss further if useful.