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Axial Spondyloarthritis Treatment Recommendations in 2024: Where Are We Now?

Sherry Rohekar, BSc, MD, FRCPC, MSc (Clin. Epi)

Introduction

As 2024 continues to evolve, so do treatment recommendations for the management of spondyloarthritis (SpA), including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). From a Canadian perspective, we eagerly await the publication of the Canadian Rheumatology Association (CRA)/Spondyloarthritis Research Consortium of Canada (SPARCC) Living Treatment Recommendations for the Management of Axial Spondyloarthritis (axSpA), currently in press. Until these recommendations for axSpA treatment with a Canadian perspective arrive – where are we now?

Current AxSpA Treatment Recommendations

There are two major treatment recommendations (or guidelines) for axSpA currently in use. The first is the 2019 Update of the American College of Rheumatology (ACR)/Spondylitis Association of America (SAA)/ Spondyloarthritis Research and Treatment Network (SPARTAN) Recommendations for the Treatment of AS and nr-axSpA.[1] The second is the 2022 update from the Assessment of Spondyloarthritis International Society (ASAS)-European Alliance of Associations for Rheumatology (EULAR) Recommendations for the Management of Axial Spondyloarthritis.[2]

In comparing the ACR and EULAR guidelines, there are some notable similarities and differences.

- ***Disease definition:*** The ACR guidelines divide SpA into distinct categories of AS and nr-axSpA, whereas the EULAR guidelines treats AS and nr-axSpA as part of the same disease spectrum, axSpA.[1,2]
- ***Non-pharmacologic interventions:*** both guidelines recommend regular exercise, patient education, and physiotherapy for maintenance of patient function and quality of life.[1,2]

- ***First-line pharmacologic therapy:*** both guidelines recommend the use of non-steroidal anti-inflammatory drugs (NSAIDs) as first-line therapy for the management of pain and inflammation in axSpA.[1,2]

- ***Biologic therapies:*** tumour necrosis factor inhibitors (TNFi) and interleukin (IL)-17 inhibitors (IL-17i) are recommended for NSAID non-responders.[1,2] In both guidelines, the use of these biologics is based on disease severity and patient-specific factors.[1,2] However, in the ACR guidelines, there is a conditional recommendation for the use of TNFi over IL-17i in adults with active AS.[1] The EULAR guidelines recommend considering the following for patients with continued high disease activity despite conventional treatment, TNFi, IL-17i, or JAK inhibitors (JAKi), with the current practice being to start either a TNFi or an IL-17i.[2] The rationale for this recommendation was the lack of safety data for JAKi at the time.[2]

- ***Biosimilars:*** the ACR guidelines strongly recommend against a mandated switch to a biosimilar TNFi in patients with stable AS.[1] In contrast, the EULAR recommendations do not directly address this issue, but state that "when a choice needs to be made between two drugs with comparable efficacy and safety, then the one with the lowest cost is preferable", noting that the rheumatologist should keep in mind the high cost of biologics to society.[2]

- ***Biologic tapering:*** The ACR conditionally recommends against tapering biologics in those with stable AS or nr-axSpA.[1] On the other hand, EULAR suggests that if a patient is in sustained remission, tapering of a biological disease-modifying anti-rheumatic drug (bDMARD) may be considered.[2]

- ***Disease Monitoring:*** The ACR guidelines conditionally recommend the regular interval use of a validated AS disease measure, but also conditionally recommend against a treat-to-target strategy of using a specific Ankylosing Spondylitis Disease Activity Score (ASDAS) over the physician's assessment.[1] Conversely, the EULAR guidelines emphasize the use of the ASDAS as the most appropriate tool for measuring disease activity, although the guidelines also acknowledged issues with the current knowledge around adopting a treat-to-target strategy.[2] Change in the ASDAS score was used as a measure of response to therapy in the EULAR guidelines' treatment algorithm.[2]

- ***Extramusculoskeletal manifestations (EMMs):*** Both guidelines recommend preferential use of a monoclonal TNFi for those with inflammatory bowel disease or recurrent uveitis, and the EULAR recommendations take a step further to suggest an IL-17i may be preferred in those with significant psoriasis.[1,2]

- ***Re-evaluating the diagnosis:*** The EULAR guidelines note that the "absence of response to treatment should prompt re-evaluation of the diagnosis and consideration of the presence of comorbidities".[2] They highlight the dangers of cycling through immunosuppressants, and the risk of overtreatment, particularly if the patient has comorbidities such as fibromyalgia, depression, or osteoarthritis that may be confounding their clinical picture.[2] They note that the increased awareness of axSpA and the rheumatologists' eagerness to decrease diagnostic delay may be leading to over treatment.[2]

- ***Use of imaging:*** The ACR guidelines conditionally recommend obtaining a spinal or pelvis MRI to assess disease activity in adults with AS or nr-axSpA who have an unclear disease activity status.[1] In the EULAR guidelines, when to re-image is included as part of their research agenda.[2]

- ***Methodology:*** The ACR guidelines use the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology.[3] This is a stringent process in which systematic literature reviews (SLRs) are conducted to answer questions using a framework that includes a predetermined clinical population, intervention, comparator, and outcomes, termed PICO. In comparison, the EULAR guidelines derive their levels of evidence and recommendation grades from SLRs, following the standards set by the Oxford Centre for Evidence Based Medicine.[4] Most treatment recommendations tend to use the more stringent GRADE approach.

Implementing Treatment Recommendations in AxSpA

Treatment recommendations are invaluable tools for clinical practice in that they help clinicians make evidence-based decisions when choosing care for their patients. However, whether these recommendations are used in daily practice remains unclear. A recent survey of axSpA treatment recommendations and disease activity monitoring in clinical practice found that though there was general awareness of the importance of disease monitoring as per guidelines, it was rarely implemented.[5] The same study showed that UpToDate ranked higher than the ACR or EULAR guidelines as a source for knowledge regarding the management of patients with axSpA.[5] What are the barriers that may be preventing the implementation of treatment recommendations in daily clinical practice?

- ***Rigidity:*** Clinicians see patients that are unique individuals who do not neatly fit into flowcharts and tables. This leads to the sense that guidelines are too restricting, and therefore not applicable to real-world practice.

- ***Overemphasis on guidelines:*** This is why I prefer to call them "treatment recommendations" – guidelines may seem like a prescriptive set of rules from the "experts" rather than from those who are faced with making day-to-day decisions. Clinicians must be allowed to tailor patient care to their own judgment.

- ***Accessibility and implementation:*** Guidelines often include recommendations that would happen in the ideal world but may be difficult to access in real life. For example, having axSpA patients with undetermined disease activity undergo reimaging with MRI is a recommendation that might be very difficult to achieve in a timely manner in some parts of Canada.

- ***Quality of evidence:*** While some of the recommendations are based on robust clinical trials, others are of low quality and largely grounded on expert opinion or consensus.

- ***Keeping pace with new evidence:*** Traditional guidelines, such as the ACR and EULAR guidelines discussed above, are almost immediately out of date upon publication. Research in axSpA is fast-paced and new modalities of treatment are emerging quickly. This leads to a lag between the guidelines and the reality of treating patients.

Living Guidelines in AxSpA

To address the issue of keeping pace with new evidence, treatment recommendations are increasingly moving to a "living guideline" model. The impending CRA/SPARCC Treatment Recommendations for AxSpA will be living guidelines. The ACR is also in the process of updating their guidelines to a living guidelines model.

What are living guidelines? In comparison to traditional guidelines, where several years pass between updates, living guidelines allow for individual recommendations to be either updated or added on an as needed basis.[6] This creates a set of guidelines that is perpetually relevant and current. In order to establish the living guidelines, a living systematic review is also simultaneously generated.[7] Supplemental journal articles or announcements may be published periodically with major modifications to the treatment recommendations to aid in knowledge dissemination. The living guideline model has already been successfully implemented for other CRA guidelines, such as rheumatoid arthritis, available **here**.[8] The living guidelines will be housed online for ease of access, and clinicians will be able to easily select their clinical question without having to read through an entire paper.

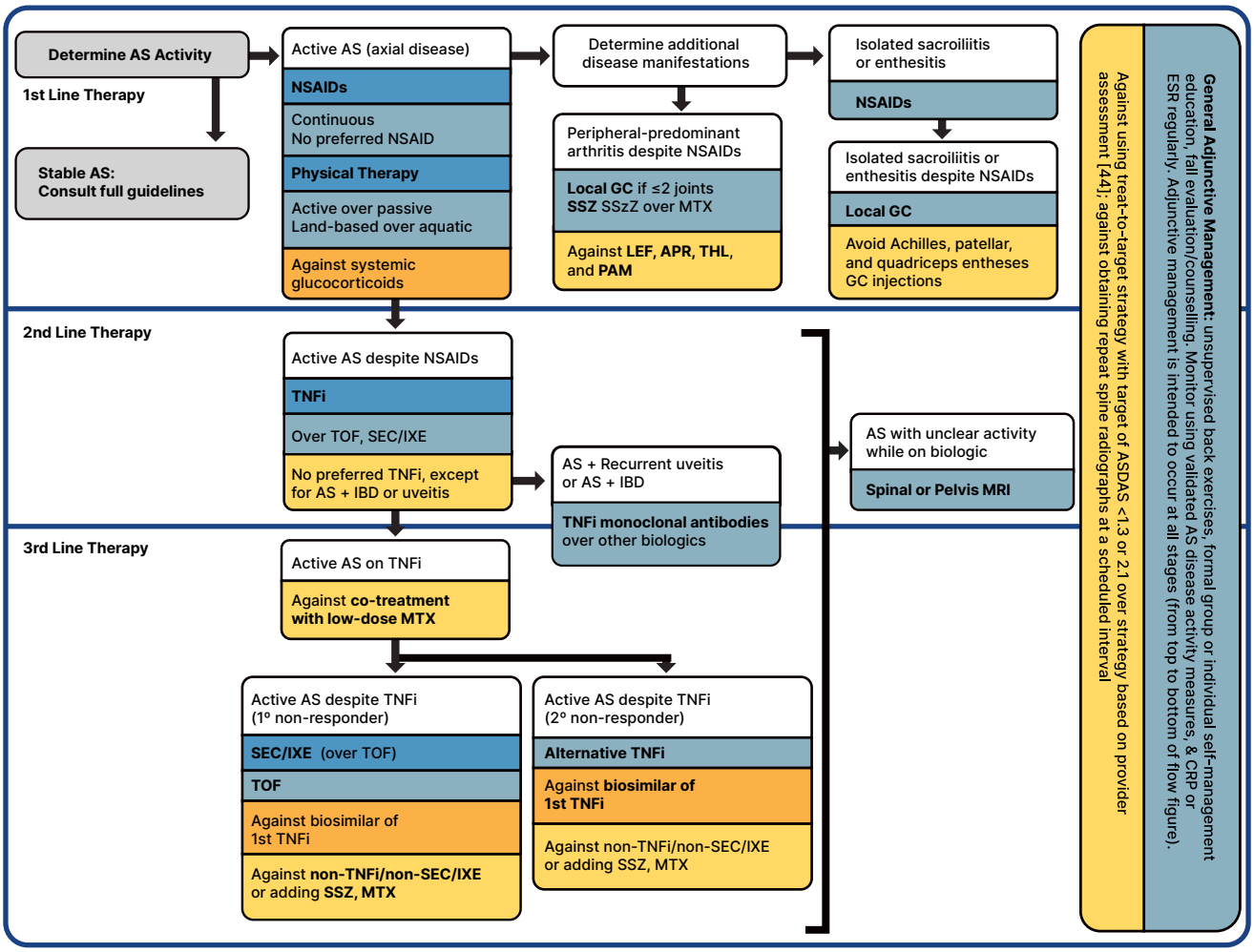

Figure 1. 2019 Update of the ACR/SAA/SPARTAN Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis**.** Summary of the main recommendations for treating patients with active ankylosing spondylitis; *adapted from Ward, MM et al., 2019*.

Abbreviations: AS: ankylosing spondylitis, **NSAIDs:** nonsteroidal antiinflammatory drugs, **GC:** glucocorticoid, **SSZ:** sulfasalazine, **MTX:** methotrexate, **LEF:** leflunomide, **APR:** apremilast, **THL:** thalidomide, **PAM:** pamidronate, **TNFi:** tumor necrosis factor inhibitor, **TOF:** tofacitinib, **SEC:** secukinumab, **IXE:** ixekizumab, **IBD:** inflammatory bowel disease, **csARD:** conventional synthetic antirheumatic drugs, **ESR**: erythrocyte sedimentation rate, **CRP:** C-reactive protein level, **ASDAS:** Ankylosing Spondylitis Disease Activity Score, **MRI:** magnetic resonance imaging, **PICO:** population, intervention, comparison, and outcomes.

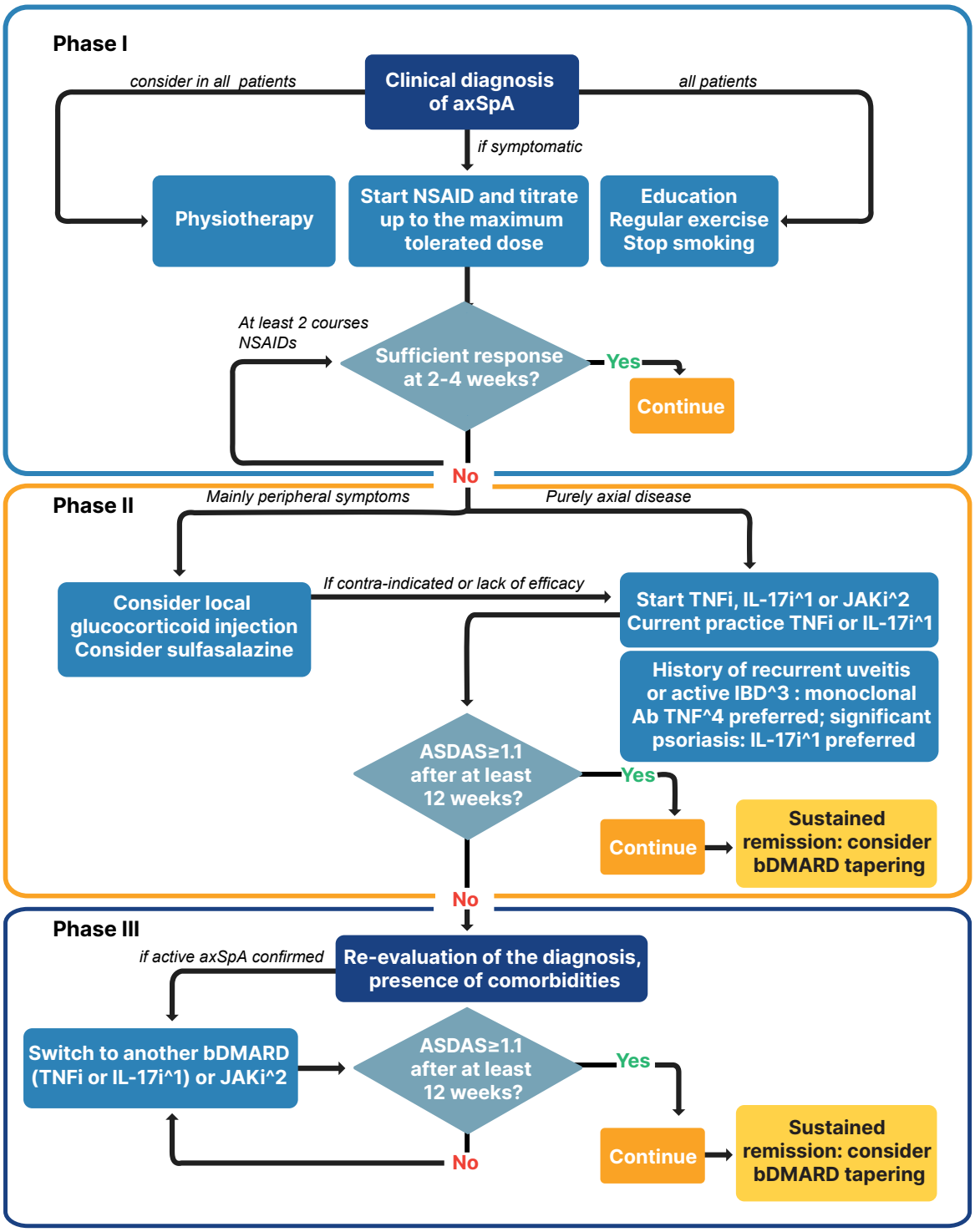

Figure 2. Algorithm based on the ASAS-EULAR recommendations for the management of axial spondyloarthritis (axSpA); *adapted from Ramiro, S et al, 2023.*

Abbreviations: Ab: antibody, **ASAS:** Assessment of Spondylo Arthritis international Society, **ASDAS:** Ankylosing Spondylitis Disease Activity Score, **bDMARD:** biological disease-modifying antirheumatic drug, **IBD:** inflammatory bowel disease, **IL-17i:** interleukin-17 inhibitors, **JAKi:** Janus kinase inhibitors; **NSAID**: non-steroidal anti-inflammatory drug, **TNFi:** tumour necrosis factor inhibitors.

Conclusion

As we progress through 2024, we can reflect on our current position to envision where we are going. Treatment recommendations for the management of axSpA will continue to be highly useful for several reasons. They will allow for standardization of care and an evidence-based approach to diagnosis, treatment, and monitoring, ensuring that clinicians are making the best therapeutic decisions for their patients. Hopefully, this in turn leads to improved patient outcomes, such as better disease control, reduced disease progression, and improved quality of life. Treatment recommendations also lend guidance on the management of comorbidities and non-pharmacologic management for our patients. Finally, they allow us to identify a research agenda by identifying gaps in our knowledge and highlighting areas for further investigation.

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