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NEWS & Views

New update on the management of axial Spondyloarthritis: Time to stop the split ten years on.

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Main text

The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) have published a new update of their recommendations for the treatment of axial spondyloarthritis. Highlights include the incorporation of newly available therapies, favouring a treatment strategy based on physician assessment rather than a treat-to-target approach and the use of imaging to aid disease monitoring. However, the guidelines artificially refer to the individual non-radiographic and radiographic disease groups rather than to a unified entity.

The recognition of axial spondyloarthritis (axSpA) as a wider entity than ankylosing spondylitis (AS), also known as radiographic axial spondyloarthritis (r-axSpA), was significantly aid by the publication of the classification criteria by the Assessment in Spondyloarthritis Society (ASAS) in 2009[1]. The contribution of these beyond the older ESSG or Amor criteria, was the recognition that unequivocal radiographic sacroiliitis, a key criterion in the modified New York criteria to define AS, is a late feature in the disease course; and that earlier disease stages may be identified by other imaging methods, chiefly MRI or a combination of key inflammatory findings such as an elevated CRP and/or associated disease features including HLA-B27. As opposed to other chronic disorders such as rheumatoid arthritis or lupus, widely accepted to have a varied clinical spectrum where a subset of patients may have a more benign or even self-limiting course, controversy is still rife as to whether earlier, non-radiographic stages in axSpA do indeed represent part of the same disease spectrum. This dispute is rooted in the absence of specific antibodies or validated biomarkers of disease which has resulted in

the artificial use of radiographic sacroiliitis as the main biomarker to identify axSpA, a problem further compounded by the well-known lack of reliability on the operator's interpretation of radiographic sacroiliitis[2] . Ten years on, the new ACR/SAA/SPARTAN[3] recommendations still outline AS and nr-axSpA as two separate diseases with individual yet similar recommendations for each. Mounting evidence however, unveils same levels of disease activity, comorbidities and treatment response[4] for nr and r-axSpA proving that their management might have to be as intensive, regardless of its classification.

The updated ACR/SAA/SPARTAN document retains non-steroidal anti-inflammatory drugs (NSAIDs) as the first-line treatment together with physical therapy. A continuous treatment rather than "on demand" is preferred both in the non-radiographic and radiographic stages, especially if the disease is active. If NSAIDs fail to provide adequate disease control, biologics should then be considered. TNF inhibitors (TNFi) are the preferred first option over IL-17 inhibitors as also outlined in the most recent 2016 ASAS-EULAR recommendations[5]. TNFi are also preferred in the presence of extra-articular manifestations such as uveitis, which can occur across the axSpA spectrum. Tofactinib, a JAk inhibitors currently under phase III trials, is also mentioned as an alternative although more data are needed to position it. Switching to IL-17 inhibitors is recommended if primary non-response to TNFi ocurrs, whilst cycling to a different TNFi is encouraged in case of secondary non-response. Overall, the advocacy for TNFi is sustained by a longer clinical experience rather than a proven superiority over IL-17 inhibitors. Added to that, real-world data are lacking on switching between treatment targets and solid knowledge on the immune-pathotype that may allow for treatment stratification remains elusive.

With the introduction of biosimilars, leading to the availability of substantially cheaper TNFi, the economic burden attached to biologic therapies has become a real consideration for rheumatologists at the time of prescribing. Ward et al[3], have conditionally recommended against switching from the originator TNFi to its biosimilar in patients with stable AS. This recommendation however has different implications depending on individual local guidelines and funding sources and cannot be extrapolated worldwide. Since several countries have pushed for switching to the TNFi biosimilar when possible, their experience will provide valuable data on its real-world interchangeability[6].

There are some stark differences between the latest ACR/SAA/SPARTAN update and ASAS-EULAR recommendations. Interestingly, the North American panel conditionally recommends against using a treat-to-target strategy based on the Ankylosing Spondylitis Disease Activity Score (ASDAS), which is

in contrast with the European recommendations[5]. The rationale behind this is the lack of hefty evidence showing the potential impact of a treat-to-target strategy on slowing radiographic progression and the risk of rapid turnaround in treatments, exhausting all available options in some patients. Although there is a recommendation on quantifying disease activity to inform treatment decisions, no outcome is proposed. The development of robust outcome measures in axSpA remains on the research agenda since available tools rely significantly on subjective measures. Importantly, it remains to be demonstrated whether the absence of a defined target might risk undertreatment in some cases.

Drug tapering has also been addressed in the 2019 ACR/SAA/SPARTAN update with a recommendation against tapering of the biologic dose as opposed to the ASAS-EULAR document where tapering was also considered and recommended. Despite literature being scarce in this field, successful tapering without significant relapses has been reported[7]. As more patients with axSpA are receiving biologic treatment and early intervention is encouraged, long term impact of continuous biologic therapy needs to be explored. In the absence of data driven definitions of remission and flare, benefits and risks of tapering have to be balanced and ultimately discussed with the patient as outlined on the 2019 ACR update.

Finally, a novelty from the 2019 ACR/SAA/SPARTAN recommendations is their advocacy for the use of magnetic resonance imaging (MRI) in patients receiving biologics where the activity of the disease is unclear and where this information would influence treatment decisions. MRI can identify active inflammation that will respond better to treatment[8] and may lead to disease progression[9]. However, the authors rightly warn about the limitations of MRI in disease monitoring particularly in view of the limited knowledge on correlation between MRI lesions and treatment response, or the significance of sub-clinical inflammatory change. Furthermore, to date, no therapies have proven to be disease modifiers in axial SpA, with only limited data showing potential effects from NSAIDS, TNFi and IL-17 inhibitors on slowing structural damage. Larger, longitudinal trials are needed to address this question.

In conclusion, the 2019 ACR/SAA/SPARTAN recommendations update the rheumatology community with useful advice on the use of new therapies and their management. Despite being formulated at addressing two distinct disease subsets: radiographic (AS) and non-radiographic, the similarities in the available evidence highlight them as part of the same clinical entity. The integration of MRI in the

evaluation of axSpA may be of value in some cases. Research efforts are needed to identify potential biomarkers and immune-phenotypes that may guide informed treatment stratification and overall understanding of axSpA[10].

Box. Highlights of the 2019 ACR/SAA/SPARTAN recommendations

- Continuous treatment with NSAIDS together with physical therapy is the preferred first-line of management in axial spondyloarthritis.
- If NSAIDS fail, biologics should be considered with a predilection for TNF inhibitors (TNFi) as a first option.
- IL-17 inhibitors are recommended when patients present a primary non-response to TNFi.
- TNFi monoclonal antibodies are preferred for treating axial spondyloarthritis with recurrent uveitis or inflammatory bowel disease.
- A treatment strategy based on physician assessment is suggested as opposed to a treat-to-target strategy.
- When the activity of the disease is unclear, magnetic resonance of the sacroiliac joints and spine can be helpful.

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