Management of Ankylosing Spondylitis: What Is Known; What Is Not Known?

Guest Editors: *Atul Deodhar, MD and Daniel O. Clegg, MD*

The last few years have witnessed remarkable progress in our understanding of the natural history, pathophysiology and, finally, several aspects of the management of ankylosing spondylitis (AS) and the associated spondyloarthritis. Included among notable advances in this field are the recent development and validation of classification criteria for "axial spondyloarthritis" and "peripheral spondyloarthritis,"[1,2] potentially allowing earlier diagnosis for the so-called nonradiographic forms of the disease, the development and validation of a new disease activity scale (Ankylosing Spondylitis Disease Activity Score)[3]; recognition of key mediators of molecular regulation of bone formation and resorption in AS (eg, DKK-1, sclerostin and Wnt proteins)[4]; and potential targets for therapy [interleukin (IL)-6, IL-17, IL-12 and IL-23, among others] as well as identification of several new genes associations (eg, IL-23R and ERAP1) linked to AS.[5] In the United States, approved therapies now include a fourth anti-tumor necrosis factor (TNF) agent (Golimumab) to treat AS.[6]

Despite these advances, however, several knowledge gaps remain in the area of management of AS. For example, the pharmaceutical armamentarium available to treat AS is much more limited than the choices available to treat rheumatoid arthritis. In contradistinction to the management of rheumatoid arthritis, there are no accepted treatment algorithms, no clear consensus as to when anti-TNF agents should be started or which patients are appropriate candidates for biologic treatment. Even less is known about how to manage patients when anti-TNF agents lose efficacy, and there are no prospective studies to decide whether treating the disease early and aggressively would improve the long-term outcome. Despite some early and provocative data on nonsteroidal anti-inflammatory drugs (NSAIDs) in structural modification,[7] we do not have a true "disease-modifying agent" in AS.[8] NSAIDs remain the foundation of AS therapy by effectively improving pain and function, but concern about their long-term safety has lead to uncertainty regarding how to use them to the best advantage of our patients. Conversely, despite minimal evidence for efficacy especially in axial disease, the disease-modifying antirheumatic drugs (DMARDs) continue to be a prescribed treatment option. Such variations in practice coupled with the above-mentioned knowledge gaps impede our abilities to most effectively manage patients.

With this background, the ninth annual meeting of the Spondyloarthritis Research and Treatment Network (SPARTAN) was held in Portland, Oregon, July 29-30, 2011. The meeting was held in conjunction with the Spondyloarthritis Research Consortium of Canada (SPARCC) and colleagues with interests in spondyloarthritis from the Pan American League of Associations for Rheumatology (PANLAR). The objective of the meeting was to perform a critical appraisal of the guidelines for the management of AS. Experts from the participating organizations were asked to critically appraise the existing guidelines for the management of AS with regard to "What is known" and "What is not known" about the following topics: NSAIDs, DMARDs, biologics, treatment strategies/economic considerations, comorbidities, imaging and clinimetrics and management of spondyloarthritis in the pediatric population. Following the presentations, meeting participants were divided into small groups for deliberation and further discussion of the presented materials. The participants of each breakout group focused their discussions on specific questions that were predeveloped to cover those aspects of management where clear guidelines were either not available (the "unknowns") or there were differing opinions. The entire meeting body then reconvened and an audience response system was used to capture the final opinions of the group on the "unknowns" as well as the key messages on each of the topics. Subsequent to the meeting, the presenting experts developed manuscripts succinctly detailing their assigned topics. These summations are included in the supplement that follows. These manuscripts represent the current state of what is known and what is not known on each of these important subjects pertaining to the management of AS in the Americas.

The July 2011 SPARTAN meeting and the publication of this supplement come at a time of transformation in the diagnosis and management of spondyloarthritis. For example, while the recently published classification criteria for axial and peripheral spondyloarthritis may promote earlier and more accurate diagnosis, and potentially result in earlier treatment of these diseases, these criteria likely define a different, or at least broader, clinical phenotype than formerly captured. Concurrently, it is becoming ever more apparent that the incidence of inflammatory back pain and spondyloarthritis is remarkably underrecognized and often undertreated.[9] SPARTAN has been instrumental in supporting these projects that clarify the epidemiology of spondylitis. In the face of higher than formerly recognized disease prevalence, and continued evidence of delays or failure to make accurate diagnoses in spondyloarthritis, it is critical that educational initiatives be developed so that rheumatologists and others who evaluate these patients readily recognize the issues hastening diagnosis and improving management. Finally, revised management guidelines have recently been published that aim to standardize and optimize the approach to effective therapy.[10] The purpose of the SPARTAN meeting and this supplement is to define the knowledge gaps that exist in spondyloarthritis management and to develop a systematic plan to effectively address these needs.

The readers of this supplement will find how the existing guidelines address the issue of the use of NSAIDs and DMARDs

From the Division of Arthritis & Rheumatic Diseases (AD), Oregon Health & Sciences University, Portland, Oregon; and Division of Rheumatology (DOG), University of Utah Health Care, Salt Lake City, Utah.

Presented at the annual research and education meeting of Spondylo-Arthritis Research and Treatment Network (SPARTAN), Portland, Oregon, July 29–30, 2011.

Correspondence: Atul Deodhar, MD, Oregon Health & Sciences University, 3181 South West Sam Jackson Park Road, Portland, OR 97239 (E-mail: deodhara@ohsu.edu).

in the management of AS as well as scholarly synthesis of available data on these agents. The article on biologic agents (TNF inhibitors) discusses how these drugs fundamentally improve the inflammatory symptoms and signs of AS as well as additional biologic targets that are actively being studied (IL-6, IL-17 antagonists, among others). The economic impact of these treatments (and delaying these treatments) is discussed herein. A thoughtful review of clinical and imaging measures is included, which is especially timely, in part, because of the important role that advanced imaging plays in the new classification criteria. Management of comorbidities that are frequently associated with spondyloarthritis is reviewed and recommendations are proposed. Similarly, management of pediatric spondyloarthritis is discussed. Finally, the roles of physical therapy and surgery in the management of AS are presented.

Developing recommendations for the world community of rheumatologists, with the ultimate goal of improving patient care, is a daunting task indeed. Rheumatology practices differ from country to country, region to region, based on access to medical care and patients' acceptance of therapy shaped by their social, financial and educational background. Although recommendations rightfully strive to be the "ideal suggested practice," to be realistically followed by the global community, they need to walk the fine line between being strictly "evidence based" and suggesting "standard practice" in situations where good quality evidence is lacking. It is our hope that this supplement will provide the community with a foundational understanding of the current state of knowledge at this important time for effective diagnosis and management of AS.

REFERENCES

1. **Rudwaleit M, van der Heijde D, Landewe R, et al.** The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis [part II]: validation and final selection. Ann Rheum Dis 2009;68:777–83.
2. **Rudwaleit M, van der Heijde D, Landewe R, et al.** The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis in general. Ann Rheum Dis 2011;70: 25–31.
3. **van der Heijde D, Lie E, Kvien TK, et al.** ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:1811–8.
4. **Schett G.** Bone formation versus bone resorption in ankylosing spondylitis. Adv Exp Med Biol 2009;649:114–21.
5. **Brown MA.** Genetics of ankylosing spondylitis. Curr Opin Rheumatol 2010;22:126–32.
6. **Inman RD, Davis JC Jr, Heijde D, et al.** Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double-blind, placebo-controlled, phase III trial. Arthritis Rheum 2008;58:3402–12.
7. **Wanders A, Heijde D, Landewe R, et al.** Nonsteroidal antiinflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: a randomized clinical trial. Arthritis Rheum 2005;529:1756–65.
8. **van der Heijde D, Landewe R, Einstein S, et al.** Radiographic progression of ankylosing spondylitis after up to two years of treatment with etanercept. Arthritis Rheum 2008;58:1324–31.
9. **Reveille JD, Witter JP, Weisman MH.** The prevalence of axial spondyloarthritis in the United States: estimates from the U. S. National Health and Nutrition Examination Survey, 2009–10 [published online ahead of print January 24, 2010]. Arthritis Care Res doi: 10.1002/acr.21621.
10. **Braun J, van den Berg R, Baraliakos X, et al.** 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011;70:896–904.