Methotrexate Not Best Option for Psoriatic Arthritis

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BOSTON — Rheumatologists need to rethink their reflex to prescribe methotrexate for psoriatic arthritis given mounting data showing that anti–tumor necrosis factor agents are more effective for this indication, Dr. Christopher Ritchlin said at a rheumatology conference sponsored by Harvard Medical School.

Although methotrexate is often the treatment of choice, "we really don't have evidence that it works for psoriatic arthritis," Dr. Ritchlin stated. "This is a very large problem. About 70%-80% of clinicians around the world who treat psoriatic arthritis say methotrexate is the first drug that they use, yet the only double-blind randomized controlled trial addressing the question was too underpowered and underdosed to make any conclusions regarding efficacy."

In addition, there is concern about liver toxicity in psoriasis patients on methotrexate—particularly because psoriasis patients tend to have higher rates of alcoholism—and there is evidence of progression of fibrosis in psoriatic arthritis patients on methotrexate, said Dr. Ritchlin of the University of Rochester (N.Y.). And, unlike with rheumatoid arthritis, there is no evidence that methotrexate is synergistic with other disease-modifying antirheumatic drugs (DMARDs) in psoriatic arthritis, he said, noting that "this is an area in which we are in desperate need of data, but it's hard to get clinical trials designed and funded."

In contrast, there is a growing body of evidence demonstrating that treatment of psoriatic arthritis with tumor necrosis factor–α (TNF-α) inhibitors safely and effectively controls disease activity at a variety of involved sites. The production of TNF-α has been shown to play a central role in the development of psoriasis and psoriatic arthritis by sustaining the inflammatory process in the skin and the joints, and anti-TNF-α agents appear to effectively block that activity, said Dr. Ritchlin.

Dr. Marte Schrumpf Heiberg of Diakonhjemmet Hospital, Oslo, Norway, has reported data from an ongoing study of the effectiveness of therapy with anti-TNF-α agents infliximab, etanercept, and adalimumab, compared with that of methotrexate in 526 patients with psoriatic arthritis. After 6 months of treatment, patients undergoing anti-TNF-α treatment showed significantly greater clinical improvement in disease measures, compared with those who received methotrexate monotherapy (Ann. Rheum. Dis. 2007;66:1038-42). Multiple studies presented at the European League Against Rheumatism meeting in June added to the growing cache of literature supporting anti-TNF-α therapy.

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Additional potential therapeutic targets for psoriatic arthritis include both B cells and T cells, as well as the interleukin-23/Th17 pathway, which is directly associated with psoriasis. Specifically, anti-p40 therapy targets an interleukin-23 subunit and has proven very effective in psoriasis treatment, according to Dr. Ritchlin

"Psoriatic arthritis, unlike rheumatoid arthritis, is quite complex in its disease manifestation," said Dr. Ritchlin. "Traditionally, it was defined as an inflammatory arthritis associated with psoriasis. However, it has become clear [it] is a systemic disease that can involve joints, gut mucosa, the uveal tract, and the endothelium, with associated cardiovascular and vascular issues."

In terms of patient management, "not only do we have to worry about peripheral arthritis, but we also have to be concerned with skin and nail disease, axial disease, dactylitis, and enthesitis," said Dr. Ritchlin. "It is critical that we approach the therapy of this disease from a global perspective, addressing all of these cardinal issues."

Clinically, however, such an approach is challenging, as the degree of involvement of each of the heterogenous areas of disease can vary substantially. Anti-TNF-α agents come closer than does methotrexate to achieving the goal of a treatment regimen that is as simple and minimally toxic as possible, said Dr Ritchlin. ■