Early Conventional Polytherapy Slows RA Course

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CHICAGO — In the era of biologically active agents for rheumatoid arthritis, it is worth remembering that early treatment with other disease-modifying antirheumatic drugs such as methotrexate, either alone or in combination, also can preserve joint architecture, usually with fewer complications and for significantly less money, Dr. James R. O'Dell said at a symposium sponsored by the American College of Rheumatology.

Evaluation of disease-modifying antirheumatic drug (DMARD) monotherapy shows that early treatment with methotrexate slows disease progression and improves survival, said Dr. O'Dell, who is professor of medicine at the University of Nebraska Medical Center in Omaha. "And the earlier the better; if we treat early, we can put a high percentage of patients in remission," he said, stressing that directing therapy at a specific target may improve outcome, as shown by the TICORA trial (Lancet 2004;364:263-9).

"They did not use biologics in the TICORA trial, but rather they ramped patients up to triple therapy. But the important thing is that they had a target, which was to accomplish a disease activity score of under 2.4, which equates to one or two tender or swollen joints. What they found was that those who got treatment with that target in mind did better," Dr. O'Dell explained.

If the patient wants to avoid side effects and lab tests, and payment is a problem, hydroxychloroquine is a good drug to consider. "It's the safest DMARD and the only test that's required is an annual eye exam," he said.

Another option is minocycline, a small-molecule medication which, like doxycycline, upregulates interleukin-10 production, and which outperformed hydroxychloroquine in a head-to-head study, the goal of which was to get patients to American College of Rheumatology rating scale (ACR) 50 in 2 years (Arthritis Rheum. 2001;44:2235-41). Caveats include the fact that minocycline's effectiveness in RA has been primarily demonstrated in seropositive patients. And in about 40% of patients treated longer than 2 years, minocycline may cause hyperpigmentation that is slow to resolve after the drug is discontinued, Dr. O'Dell cautioned.

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DR. O'DELL

Another option is azathioprine, which Dr. O'Dell called "a sort of forgotten drug. We use this in combination with methotrexate because it's effective and affordable for people with high copays."

Combinations of DMARDs also preserve joints in RA. Tested combinations include:

- Triple therapy with methotrexate, sulfasalazine, and hydroxychloroquine.
- Sulfasalazine, methotrexate, and high-dose prednisone (COBRA combo).
- Methotrexate and the tumor necrosis factor–α (TNF-α) inhibitors.

Combination therapy (methotrexate, sulfasalazine, and hydroxychloroquine) was pitted against monotherapy (any one of these drugs) in what Dr. O'Dell called a somewhat obscure Turkish study. "What they showed was that three drugs are better than two and two drugs are better than one. In the three-drug group, 69% of patients had no radiographic progression, compared with 64% in the two-drug group and 24.5% in the monotherapy cohort," he said (Clin. Exp. Rheumatol. 1999;6:699-704).

More recently, the PREMIER study of adalimumab and methotrexate alone or in combination showed that combining drugs was the best thing to do (Arthritis Rheum. 2006;54:26-37). "More drugs are better than fewer drugs if what you're striving for is efficacy. When we look at ACR 50, the two drugs alone were similar. However, achievement of ACR 20 statistically favored methotrexate (over the TNF inhibitor) and that's interesting," explained Dr. O'Dell, adding that those taking a combination of the two drugs had the best clinical responses and the least radiographic progression. Of those PREMIER patients on combination therapy, 61% had no radiographic progression. However, the benefits came at a cost: Those receiving the TNF inhibitor had a significant increase in serious infections.

The side effects of TNF inhibitors, underscore the importance of screening patients for tuberculosis and other infections before placing them on these biologics, Dr. O'Dell stressed. "Infections are a concern … and if we hide our heads in the sand, we're doing our patients a disservice. These are extremely effective drugs, but we just need to take appropriate precautions." ■

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