In Primary Anti-TNF Failure, Switch It Up

BY SALLY KOCHE KUBETIN
EXPERT ANALYSIS FROM A RHEUMATOLOGY SEMINAR

SANTA MONICA, CALIF. – Rheumatoid arthritis patients with a true primary failure on a first-time trial of tumor necrosis factor inhibitor therapy should change to treatment with a biologic that has a different mechanism of action. The likelihood is great that trying a second anti-TNF agent will result in a different outcome. At least half of the patients who develop adverse events from treatment with a first anti-TNF agent will not improve efficacy (Arthritis Rheum. 2008;58[suppl.]:abstract 999).

Evidence that treating to target in RA is effective dates back to 1998, and this therapeutic approach has become more important in the biologics era of care. The goals of treating to target, as outlined by ACR/EULAR, are to aim for complete remission of low disease activity; to see the patient monthly for at least the first 3-6 months, depending on disease activity; to use a combination of validated response measures; to consider comorbidities; to have an increased awareness of remission; and to get informed consent.

So how does one tell whether a patient’s lack of response to an anti-TNF agent is a true primary failure or is secondary to something else that may be correctable, such as a longer therapeutic trial? Findings from a secondary analysis of TEMPO (Trial of Etanercept and Methotrexate With Radiographic Patient Outcomes) data show that about half of the patients who had not responded by 12 weeks to treatment with etanercept or methotrexate, either as monotherapy or in combination, were still likely to respond by 24 weeks with either treatment (Ann. Rheum. Dis. 2008;67:1444-7).

“If there is a hint of a response, treat beyond the usual 12 weeks,” advised Dr. Daniel E. Furst, who is the Carl M. Pearson Professor of Medicine at the University of California, Los Angeles. Some patients may need a higher dose of the anti-TNF agent than they have been receiving. A chart review presented by Dr. Furst and colleagues at the 2008 annual meeting of the ACR showed that increasing the adalimumab dose from 40 mg subcutaneously every other week for 5 months to 40 mg every week for 6 months can increase the number of patients with good EULAR responses. Of 48 patients who originally had received 40 mg of adalimumab subcutaneously every other week for 5 months, 20 had good response and 28 achieved moderate or no EULAR responses. An increase in the dose to 40 mg every week for 6 months resulted in a good EULAR response in 8 of 28 nonresponders, which included 4 of 12 patients who originally had no response to the lower-dose adalimumab (Arthritis Rheum. 2008;58[suppl.]:abstract 999).

One can improve treatment response to infliximab by decreasing the interval between doses. But increasing the dose and leaving the interval the same does not have the desired effect. Other data from Dr. Furst’s research suggest that in the case of etanercept, increasing dose does not improve efficacy (Arthritis Rheum. 2007;56[suppl.]:abstract 726).

Higher doses of anti-TNF agents are associated with higher rates of nonserious adverse events, especially with adalimumab and infliximab. Data from pack-inserts show that infliximab has a 5.3% rate of serious adverse events, which is higher than that seen with adalimumab (2%), etanercept (1%), golimumab (1.9%), and certolizumab (3%). Data from the French RATIO registry show that, during 57,711 people-years of biologic use in 2004-2007, there were 69 cases of tuberculosis in patients who took anti-TNF agents for a variety of reasons, including RA. After adjustment for confounding risk factors, the incidence rate for TB in patients taking any anti-TNF drug was shown to be 116.7 cases per 100,000 person-years of use (Arthritis Rheum. 2009:60:1884-94).

The bottom line is that not only are anti-TNF agents less effective after a primary failure, but the rate of adverse events increases as well, judging from data reported at the annual meeting of the European League Against Rheumatism in 2008 by Dr. Luba Nalysnyk of United BioSource Corp. Dr. Nalysnyk noted that 53 of 169 (31.4%) of the meta-analysis of 16 articles and 15 abstracts involving 5,306 patients. In the meta-analysis, primary failure of an anti-TNF agent occurred in 48% of patients. A second anti-TNF agent did not work in 66% of those patients, and another 66% of those patients developed adverse events in response to the second agent. SDEF and RHEUMATOLGY NEWS are owned by Elsevier. Dr. Furst has disclosed financial relationships with Abbott, Actelion, Amgen, Array, Biogen Idec, BMS, Celgene, Centocor, Genentech, Gilead, GSxK, the National Institutes of Health, Nitace Pharma, Novartis, Roche, UCB, and Wyeth.

Biologic Agent Improved Sleep in Ankylosing Spondylitis

BY SHARON WORCESTER
FROM ARTHRITIS CARE AND RESEARCH

The anti-tumor necrosis factor-α agent golimumab significantly reduced sleep disturbance and improved health-related quality of life in a randomized placebo-controlled trial of 356 patients with ankylosing spondylitis.

The investigators assessed sleep disturbance using the Jenkins Sleep Evaluation Questionnaire (JSEQ), which asks patients how many times in the past month they have had trouble falling asleep, awakened several times, and improved health-related quality of life in a randomized placebo-controlled trial of 356 patients with ankylosing spondylitis.

One randomized placebo-controlled study of 356 patients with ankylosing spondylitis showed that increasing the adalimumab dose from 40 mg subcutaneously every other week for 5 months to 40 mg every week for 6 months can increase the number of patients with good EULAR responses. Of 48 patients who originally had received 40 mg of adalimumab subcutaneously every other week for 5 months, 20 had good response and 28 achieved moderate or no EULAR responses. An increase in the dose to 40 mg every week for 6 months resulted in a good EULAR response in 8 of 28 nonresponders, which included 4 of 12 patients who originally had no response to the lower-dose adalimumab (Arthritis Rheum. 2008;58[suppl.]:abstract 999).

Major Finding: Compared with patients in the placebo group, those in the golimumab groups had significantly greater median improvement from baseline on the 0- to 20-point JSEQ at 14 weeks’ follow-up (−3.0 vs. 0.0 point change), and the improvement was sustained at 24-week follow-up (−3.0 vs. −1.0 point change).

Data Source: Randomized, placebo-controlled study of 356 patients with ankylosing spondylitis.

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