

Consensus Statement on Biologics Updated

BY LEANNE SULLIVAN

New data have prompted an update of a widely cited consensus statement on biologic agents for rheumatic arthritis, psoriatic arthritis, ankylosing spondylitis, and other rheumatic diseases, according to Dr. Daniel E. Furst and the other members of the international expert panel that revised the document.

The addition of biologics to the treatment options for rheumatic diseases has greatly improved outcomes, and research continues on the best use of these agents. The panel, made up of rheumatologists from universities in Europe, North America, South America, Australia, and Asia, cited new findings encompassing tumor necrosis factor (TNF)-alpha blocking agents, abatacept, rituximab, tocilizumab, and interleukin 1 (IL1) receptor antagonists.

TNF-Alpha Blockers

The TNF-alpha blockers infliximab, adalimumab, and etanercept are most often used for rheumatoid arthritis in combination with other disease-modifying antirheumatic drugs (DMARDs) such as methotrexate. New evidence has indicated that combining methotrexate with a TNF-alpha inhibitor is more effective for RA than is a combination of DMARDs without a TNF-alpha blocker, according to the new consensus statement (*Ann. Rheum. Dis.* 2010;69[suppl 1]:i2-29).

The dose of TNF-alpha blockers can be lowered during times of RA remission or low disease activity without loss of effectiveness, according to the update. Also, one TNF-alpha blocker may be substituted for another that has stopped working for RA, according to one randomized, controlled trial and several retrospective, observational studies cited by Dr. Furst, the Carl M. Pearson professor of medicine at the David Geffen School of Medicine, of the University of California, Los Angeles, and his coauthors.

In patients with psoriatic arthritis, all of the approved TNF-alpha blockers have been shown to be equally effective. Golimumab was approved for this indication since the last consensus statement on biologic agents was released.

In ankylosing spondylitis, regular infliximab therapy was more effective than "on demand" therapy. Adding methotrexate to infliximab did not increase effectiveness of treatment, the update noted.

Cardiovascular events decreased in patients taking TNF-alpha blockers, according to the results of several new studies. Although previous studies found a link between TNF-alpha blockers and a higher risk of solid tumors, subsequent analyses of the same data found no link.

Caution and repeat testing should be used when these agents are used in populations with a high prevalence of tuberculosis. Some evidence suggests that TNF-alpha antagonist therapy can be reinitiated following TB treatment.

TNF-alpha blockers have been associated with the development or exacerbation of psoriasis, but prescribing a different TNF-alpha blocker may resolve the problem, according to the update.

Abatacept

New evidence suggests that in methotrexate-naive patients with early RA, initiating treatment with methotrexate plus abatacept is more effective than using methotrexate plus placebo, Dr. Furst and his colleagues wrote.

Autoimmune disease incidence was not increased with abatacept, according to the clinical trial database for the drug.

Recent evidence supports earlier findings that abatacept use decreased response to vaccinations for influenza, pneumococcal, and tetanus infections, so the previous recommendation that live vaccines not be used within 3 months of abatacept treatment remains valid.

Rituximab

Clinical trials have shown that rituximab

Recommendations Are Evolving

MY TAKE

This consensus statement remains an evolving document as the state of research and appearance of new drugs require constant updating. This statement represents a good, data-based statement supplemented by findings gathered from reports of worldwide experience with these agents and expertise from about 150 recognized experts.



DR. FURST

One important aspect of the statement is that the level of evidence for the recommendations is included, allowing readers to judge the document in context. The recommendations can be a focus

for local statements by the European Union as well as Central and South American countries.

The statement also offers a resource for off-label drug use, because it contains extensive appendices of documented off-label use of biologic agents.

DANIEL E. FURST, M.D., the Carl M. Pearson professor of medicine at the David Geffen School of Medicine, University of California, Los Angeles, is the lead author on the updated consensus statement on biologic agents for the treatment of rheumatic diseases, 2009.

can slow radiographic progression of rheumatoid arthritis for up to 2 years. Also, after one or more TNF-alpha blockers have been ineffective, rituximab has been shown to be more effective than another TNF-alpha inhibitor, according to the update on biologic agents.

Rituximab is contraindicated in patients with hepatitis B infection, as fatal HBV reactivation has been reported with its use in non-Hodgkin's lymphoma patients. Risk of other serious infections did not increase with repeated courses of the drug, and did not increase in patients who received another biologic after rituximab.

Like abatacept, rituximab decreased the immune response to pneumococcal vaccine, but unlike abatacept, it did not decrease response to tetanus vaccine. However, live vaccines should be given before rituximab, the update authors said.

Tocilizumab

Recent studies showed that tocilizumab, used alone or in combination with methotrexate for rheumatoid arthritis in

patients with an unsatisfactory response to DMARDs or TNF-alpha blockers, did not increase rates of cardiovascular events or cerebrovascular accidents.

However, the update said that tocilizumab has been linked with cases of peritonitis, lower GI perforation, fistulae, and intra-abdominal abscess. Hepatic failure and liver damage have not been reported, but liver function should be monitored because of increased bilirubin levels with this drug.

IL1 Blockers

Anakinra is the only IL1 blocker approved for the treatment of RA in the United States. Riloncept has been approved for cryopyrin-associated periodic syndromes, but is clinically effective in only a few patients with the autoinflammatory syndrome.

Anakinra did not interfere with the effectiveness of tetanus vaccine, according to the findings of one controlled trial.

The authors said they had no conflicts of interest pertaining to the update. ■

Criteria Narrowed to Aid SpA Referral in Primary Care

BY MITCHEL L. ZOLER

PHILADELPHIA — A set of either five or six criteria helped physicians identify patients with back pain who had a high likelihood of having spondyloarthritis in a German study.

The number of helpful criteria varied depending on whether patients underwent testing for HLA-B27, Annalina Braun said at the annual meeting of the American College of Rheumatology. When the assessment included testing for HLA-B27 positivity, a total of six assessment criteria proved helpful: back pain that improves with movement but doesn't improve with rest, pain that im-

proves within 48 hours on treatment with an NSAID, age of pain onset of 35 or less, alternating buttock pain, a history of enthesitis, and a positive HLA-B27 test.

Patients who met at least three of these six criteria had spondyloarthritis (SpA) with a sensitivity of 79% and a specificity of 60%, and 76% of all SpA cases in the validation cohort of the study had correct classification, said Ms. Braun, a researcher at the Rheumazentrum Ruhrgebiet in Herne, Germany.

The study run by Ms. Braun and her associates included 950

patients with back pain seen during April 2007–June 2009.

When HLA-B27 status wasn't included as part of the primary



The presence of four criteria identified SpA patients with a sensitivity of 48% and a specificity of 86%.

MS. BRAUN

care assessment, a set of five criteria had the best performance for case identification. Four of those were identical to those in the prior set: back pain that improves with movement but not

rest, pain that improves within 48 hours on NSAID treatment, age of onset of 35 or less, and alternating buttock pain. Awakening during the second half of the night because of back pain rounded out this list. In Ms. Braun's study, the presence of at least four of these five criteria identified SpA patients with a sensitivity of 48% and a specificity of 86%, and accounted for 71% of SpA cases in the validation cohort studied.

A group of 36 rheumatologists then performed a follow-up assessment on 322 of these patients a median of 20 days following their initial examination. The average age of the 322 patients was 36, with a range of

17-55. The median duration of back pain was 2.5 years.

The rheumatologists diagnosed axial SpA in 113 of the 322 patients (35%). Ms. Braun and her associates then analyzed which diagnostic criteria initially assessed by the orthopedic surgeons correlated best with the SpA diagnoses rendered by the rheumatologists. These case-ascertainment criteria now need validation in additional patient populations, Ms. Braun said.

The study was supported by an unrestricted grant from Abbott Germany. One of the coauthors is an employee of Abbott Germany; Ms. Braun and the other coauthors had no disclosures. ■