Etanercept Bests Sulfasalazine for Treating AS

BY MITCHEL L. ZOLER

COPENHAGEN — Etanercept was better than sulfasalazine for improving clinical symptoms in patients with ankylosing spondylitis, regardless of whether they had peripheral joint involvement.

"These findings support the role of etanercept as a key therapy for the management of subjects with AS [ankylosing spondylitis] regardless of peripheral joint involvement," Dr. Jürgen Braun and his associates reported in a poster at the annual European Congress of Rheumatology.

The results help further solidify the role of tumor necrosis factor (TNF) inhibitors as the standard of care for treating AS, Dr. Braun said in an interview. Until recently, when TNF inhibitors became established as prime agents for treating AS, sulfasalazine had been the most widely used drug in this disorder, said Dr. Braun, director of the regional rheumatology center at St. Josefs Hospital in Herne, Germany.

The new analysis used data collected from 566 patients with active AS who had failed treatment with a NSAID. The study randomized them to either etanercept (Enbrel) 50 mg subcutaneously once weekly or up to 3 g sulfasalazine daily. The study's primary end point was the percentage of patients having a 20% or better improvement from baseline in their disease state, as measured by ASAS (Assessment of AS International Society) 20 criteria, after 16 weeks of treatment. The study was done at several centers in 15 European countries and in China.

The study was sponsored by Wyeth, the company that markets etanercept. Dr. Braun said that he was on the speakers bureau of and received grants from "all companies that sell biologics in the field of SpA." His coauthors all served as speakers for, received grants from, or were employees of Wyeth.

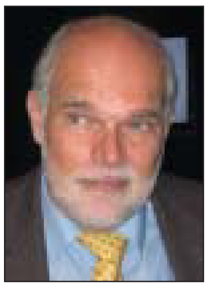
Dr. Braun and his associates reported results for the entire group of 566 patients last October at the annual meeting of the American College of Rheumatology.

An ASAS 20 response occurred in 76% of 379 patients treated with etanercept and in 51% of 187 patients treated with sulfasalazine, a statistically significant difference (Arthritis Rheum. 2008;58:S415).

In their most recent report on these data at the EULAR Congress, the researchers updated the ASAS 20 response in sulfasalazine-treated patients to 53%, still significantly less than the 76% rate in those treated with etanercept.

Further assessment in a post hoc analysis divided the patients into a group of 374 without swollen peripheral joints, and a group of 181 with at least one swollen peripheral joint. (Joint status wasn't available for the other 11 patients in the study.)

Among the patients with peripheral joint swelling, an ASAS 20 response was still significantly more common in those treated with etanercept (69%) than in those treated with sulfasalazine (50%), they reported in their poster. A significant difference in favor of etanercept also appeared in the subgroup of patients without peripheral joint swelling.



Figures reported at the EULAR Congress show 76% of patients responded to etanercept, 53% to sulfasalazine.

DR. BRAUN

Etanercept was significantly better than sulfasalazine among both subgroups for all of the other efficacy measures reported, including achievement of partial remission, and improvement of several of the Bath AS clinical measures, including the Bath AS Disease Severity Index.

The emergence of etanercept and other TNF inhibitors as substantially more effective than sulfasalazine for treating AS has been a major advance in AS treatment. Although sulfasalazine has been, until recently, the most commonly used drug, it never achieved an anchor role for AS, as methotrexate has for treating rheumatoid arthritis, Dr. Braun said in the interview. The ASAS is now in the process of updating its AS treatment recommendations, which the group last issued in 2005. The updated recommendations should be released by the end of this year, Dr. Braun said. ■

ASK THE EXPERT

ACR/EULAR Criteria Streamline Early RA Management

The management of rheumatoid arthritis has changed dramatically over the past several years as rheumatologists have begun advocating early, aggressive treatment with combination disease-modifying antirheumatic drug regimens and biologic agents to prevent structural joint damage and loss of function.

JONATHAN KAY, M.D.

With the introduction of new therapies that can halt the disease in its earliest stages, the shortcomings of the American College of Rheumatology classification criteria—the de facto disease classification standard since its adoption in 1987—have become ever more glaring.

The result has been cries for a revised tool designed to identify early arthritis before the occurrence of irreversible, erosive structural damage.

Toward this end, a joint task force assembled by the European League Against Rheumatism and the ACR has developed a new classification system that will allow for earlier diagnosis of rheumatoid arthritis.

The new classification system also promises to change the paradigm of drug development and testing, according to ACR board liaison and task force member Dr. Jonathan Kay.

In this month's column, Dr. Kay of the University of Massachusetts Medical Center in Worcester provides a sneak peak into the forthcoming ACR/EULAR diagnostic criteria for rheumatoid arthritis, which are slated for formal release this month at the ACR annual meeting in Philadelphia.

RHEUMATOLOGY NEWS: Can you describe the need for the new diagnostic criteria?

Dr. Kay: The 1987 ACR criteria were developed based on patients with established disease, and were designed to discriminate these patients from those with other rheumatologic disorders. Thus, they include items such as erosions, which are not necessarily present early on in RA patients. Also, the 1987 criteria do not include newer serologic markers, such as antibodies to cyclic citrullinated peptides [anti-CCP], which now are widely used clinically for diagnosing RA.

What we have been lacking are criteria that can classify patients with RA early in the course of the disease. The new criteria mirror the process rheumatologists who are expert in the diagnosis and management of RA use to make management decisions, based on their clinical experience and clinical impression. Basically, the new criteria codify the thinking of experienced rheumatologists. These criteria will facilitate earlier diagnosis and will allow the prompt initiation of appropriate treatment. These criteria also will allow us to define RA at an early stage and facilitate the inclusion of these patients in clinical trials.

RN: With respect to design, how do the new criteria differ from the 1987 ACR criteria?

Dr. Kay: The new criteria are based on a system whereby different scores are assigned to different diagnostic elements and a total score is calculated. If the total number of points accumulated exceeds a specific cutoff, the diagnosis of RA can be made. The various diagnostic elements are derived from each of several different clinical domains, including the pattern and extent of joint involvement, duration of symptoms, blood levels of C-reactive protein, erythrocyte sedimentation rate, and specific serologic markers, such as rheumatoid factor and anti-CCP antibodies.

The criteria are very easy to use. 'As a clinician I find the criteria to be valid and very easy to apply to patients, both in the context of clinical practice and for clinical studies.'

RN: How were the criteria developed?

Dr. Kay: In the first phase, a group of experienced rheumatologists from the United States, Canada, and Europe used a data-driven approach to carefully analyze cohorts of patients with early inflammatory arthritis. This group identified clinical features that correlated with the initiation of methotrexate therapy to prevent the development of joint erosions, which was the surrogate for making a diagnosis of rheumatoid arthritis. Subsequently, using an evidence-based, consensus-driven approach, the group reviewed a set of cases drawn from clinical practice and each expert clinician independently scored each case based on the probability that methotrexate therapy would be initiated to prevent the development of erosions. Proprietary decision-analysis software was used to compare each of the different diagnostic elements considered in the decision process, and relative weights were assigned to each element in each domain.

RN: Were there any surprises?

Dr. Kay: Surprisingly, symmetry of joint involvement was not a significant discriminating factor in determining the diagnosis of RA.

RN: How easy will it be to integrate the new criteria into clinical practice and clinical trials?

Dr. Kay: The criteria are very easy to use. Basically, one goes down the list of clinical features, identifying which items pertain to the patient in question, and sums the individual scores for each domain. As a clinician, I find the criteria to be valid and very easy to apply to patients, both in the context of clinical practice and for clinical studies.

—Diana Mahoney

DR. KAY *is the director of clinical research and professor of medicine at the University of Massachusetts in Worcester.*