Pegloticase Improved Function in Refractory Gout

BY MITCHEL L. ZOLER

COPENHAGEN — Patients with refractory chronic gout who were put on pegloticase had statistically significant and clinically meaningful improvements in their health-related quality of life after 25 weeks of treatment in two placebo-controlled studies with a total of 157 patients.

Refractory chronic gout accounts for a small subset of patients with gout (about 1%-2%) who have significantly lower health-related quality of life scores than do age- and sex-matched norms. Combined results from two similar studies of the investigational drug pegloticase showed that, in addition to significantly cutting disease activity and pain, the pegloticase regimen improved other physical and mental domains and resulted in normal or near-normal values in more than half the domains measured on the SF-36 (Medical Outcomes Study 36-Item Short Form Health Survey), Dr. Vibeke Strand said at the annual European Congress of Rheumatology. About 50,000 Americans have treatment-resistant gout, she estimated.

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"We never before had gout patients report feeling better by function, global assessment, pain, and health-related quality of life, so it's a very clinically meaningful result," Dr. Strand said in an interview. "Treatment-failure gout affects not just the physical domains, but the mental domains, too."

Savient Pharmaceuticals Inc. announced on Aug. 2 that the Food and Drug Administration had notified the company that its intravenous drug pegloticase, under review for treating chronic gout in refractory patients, could not be approved at this time, partly because of manufacturing issues. The company plans to meet with the agency to address these issues, according to the statement.

Without pegloticase treatment, patients with refractory chronic gout have an average health-related quality of life (QOL) that's worse than that of patients with osteoarthritis and hypertension, and worse than that of patients with angina and hypertension, said Dr. Strand, a rheumatologist at Stanford (Calif.) University. The severity of their health-related quality of life is comparable to that of patients with long-standing rheumatoid arthritis and patients with active systemic lupus erythematosus, she added.

Dr. Strand and her associates measured improvements in quality of life in 157 of the 212 total patients enrolled in two similar trials, the GOUT (Gout Outcomes and Uric Acid Treatment) 1 and GOUT 2 studies. Both studies randomized patients with treatment-resistant gout to treatment with 8 mg pegloticase administered by a 2-hour IV infusion every 2 weeks, 8 mg pegloticase infused once every 4 weeks, or placebo. Treatment continued for 25 weeks.

Pegloticase is a pegylated form of a modified, mammalian urate oxidase. The study was funded by Savient Pharmaceuticals, which is developing pegloticase (Krystexxa). Dr. Strand reported receiving research support from and serving as a consultant to Savient.

The primary outcome of the pivotal GOUT 1 and GOUT 2 studies was the proportion of patients with normalization of their plasma uric acid level during the final 3 months on treatment. Data in prior reports showed that this was significantly boosted by pegloticase treatment in these two studies.

The new analysis examined data collected at baseline and after 25 weeks on treatment from the SF-36 (with eight domains) and the HAQ-DI (Health Assessment Questionnaire–Disability Index). Baseline levels showed SF-36 domain scores that were 15-30 points (on a 0-100 scale) below U.S. normative levels. The HAQ-DI scores reflected moderate to severe levels of disability, Dr. N. Lawrence Edwards, Dr. Strand, and their associates reported in a poster presented at the congress.

For example, scores in the physical function domain averaged 45 in the 212 patients with refractory chronic gout, compared with 60 in age- and sex-matched norms. Average mental health domain scores were 68 in patients vs. 79 in age- and sex-matched norms.

The average domain scores in the gout patients who were enrolled in the two pegloticase studies were similar to the average SF-36 domain scores in a longitudinal study of 110 patients with refractory chronic gout, and in a third study of about 1,500 Veterans Affairs patients with gout, according to a second report at the meeting by Dr. Strand.

The 85 patients in GOUT 1 and GOUT 2 who received pegloticase every 2 weeks had "clinically-meaningful" improvements in their average SF-36 scores for all eight domains, reported Dr. Edwards, professor of rheumatology at the University of Florida in Gainesville, and his associates in their poster. Improvements, compared with baseline, were greatest for bodily pain, physical functioning, physical role, and social functioning. Pegloticase every 2 weeks for 25 weeks led to normal or near-normal average scores for five domains: bodily pain, mental health, emotional role, social functioning, and vitality. Pegloticase also produced significant improvements in HAQ-disability index scores.

Dr. Edwards said that he received research support from Savient. ■

New Peripheral SpA Criteria Improved on Existing Schemes

BY MITCHEL L. ZOLER

COPENHAGEN — New criteria for diagnosing peripheral spondylarthritis from the Assessment of Spondyloarthritis International Society had a higher sensitivity and specificity than did either of the diagnostic schemes currently used.

The new criteria "performed well in patients with predominantly peripheral manifestations [of spondyloarthritis (SpA)], and appeared to be better balanced in [this] study" than were the two diagnostic formulas most often used today: the system of the European Spondylarthropathy Study Group (ESSG), and the system developed by Dr. Bernard Amor, said Dr. Martin Rudwaleit at the annual European Congress of Rheumatology. Both the ESSG and the Amor criteria were first introduced nearly 20 years ago.

"I assume that, in the past, many patients who were thought to have undifferentiated arthritis had, in fact, SpA. These patients will be better captured with the new criteria. The new criteria were designed to help rheumatologists [who are] less experienced with SpA," said Dr. Rudwaleit, a rheumatologist at Charité University Hospital Berlin and a member of the Assessment of Spondyloarthritis International Society (ASAS).

The new peripheral SpA criteria complement the new ASAS criteria, published in June, for diagnosing predominantly axial SpA (Ann. Rheum. Dis. 2009;68:770-6;777-83).

The major difference between the new peripheral SpA criteria and the ESSG and Amor criteria is the addition of positivity for HLA B27 as a strong determinant of SpA, along with peripheral arthritis, enthesitis, or dactylitis, Dr. Rudwaleit said in an interview. "HLA B27 is an important marker for SpA."

Many rheumatologists who specialize in SpA "would say that if a patient has peripheral arthritis and has HLA B27, and if you rule out other possibilities such as peripheral rheumatoid arthritis, then they have SpA, and this is really new for the criteria. It's probably why the sensitivity was better. The ESSG misses these patients because in them HLA B27 has no role. In the Amor criteria, peripheral arthritis and HLA B27 without additional SpA features do not suffice for classifying a patient with SpA."

Among the patients who were used to test the criteria, HLA B27 occurred in 46% of those diagnosed with SpA by the experts, compared with 6% of patients who were not diagnosed with SpA.

To develop the new peripheral SpA diagnostic criteria, the ASAS invited its membership of about 100 rheumatologists to participate; 28 members were actively involved. They developed two slightly different sets of criteria that they then tested using a multicenter series of 266 patients with predominantly peripheral arthritis of the SpA type.

Each participating ASAS rheumatologist carefully examined each peripheral arthritis patient at his or her institution, and determined a "gold standard" diagnosis of either SpA or not-SpA, based on experience and judgment. They diagnosed 176 patients (66%) with SpA; the remaining 90 patients didn't have SpA, the experts said. Each patient was then assessed by both of the new, draft ASAS criteria sets, as well as by the ESSG and Amor criteria.

The ASAS criteria set that performed best is useful in diagnosing peripheral SpA in patients who present with peripheral arthritis of the SpA type (asymmetric, lower limb, or both), enthesitis, or dactylitis, plus at least one additional feature from list 1, or at least two additional features from list 2. (See box.)

When applied to the 266 test patients and compared with the diagnosis of each patient by the consulting ASAS experts, the ASAS criteria had a sensitivity of 75% and specificity of 82%. In contrast, the ESSG criteria had a sensitivity of 55% and a specificity of 81%, the Amor criteria had a sensitivity of 35% and a specificity of 98%, and the alternative ASAS criteria had a sensitivity of 63% and a specificity of 90%, Dr. Rudwaleit reported.

The new ASAS criteria will be published toward the end of the year.

Dr. Rudwaleit said that he and his associates had no relevant conflicts of interest to disclose. ■

ASAS Criteria for Peripheral SpA

Patients need to have peripheral arthritis (asymmetric, lower limb, or both), enthesitis, or dactylitis, plus either:

At least one of these features:
Crohn's disease
HLA B27
Preceding infection
Psoriasis
Sacroiliitis on MRI/x-ray imaging
Uveitis

Or at least two of these features:
Arthritis
Dactylitis
Enthesitis
Family history of spondyloarthritis
Inflammatory back pain

Source: Dr. Rudwaleit