

New Therapies Step Up to the Plate for Gout

BY NANCY WALSH
New York Bureau

FORT LAUDERDALE, FLA. — The likely approval of febuxostat for treating gout means there soon will be an alternative for the underserved group of patients with severe disease who cannot tolerate allopurinol.

No new urate-lowering treatments for gout have been approved since 1964, but late last year the advisory panel of the Food and Drug Administration (FDA) voted 12-0, with 1 abstention, in favor of approval for this nonpurine selective xanthine oxidase inhibitor. The FDA usually follows the recommendations of its advisory panel.

Experience to date with febuxostat in more than 4,000 patients has shown that, unlike with allopurinol, there appears to be no need for dose adjustment in patients with mild to moderate renal dysfunction. Dosage concerns exist for pa-

tients with renal insufficiency taking allopurinol, because of the possible occurrence of toxic epidermal necrolysis, said Dr. Robert L. Wortmann, professor of medicine, Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

There also have been no reports of hypersensitivity reactions, even in patients who previously had such reactions to allopurinol, most likely because of the two drugs' differences in structure, Dr. Wortmann said at a meeting sponsored by RHEUMATOLOGY NEWS and Skin Disease Education Foundation.

In a phase III clinical trial, 81% of pa-



This proton density image shows a low to intermediate signal tophus.

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tients receiving 80 mg febuxostat per day had serum urate levels below 6 mg/dL after 52 weeks of therapy, compared with 39% of patients receiving 300 mg allopurinol per day (N. Engl. J. Med. 2005;353:2450-61).

Although not all patients can tolerate allopurinol, that drug also is effective. However, it often is not prescribed in sufficiently high doses, according to Dr. Wortmann, who is a consultant to Takeda Pharmaceutical Co., the manufacturer of febuxostat. The drug is approved for doses up to 800 mg/day.

The goal of antihyperuricemic therapy is to lower the serum urate to 5-6 mg/dL.

"If you lower the urate from 12 mg/dL to 7 or 7.5 mg/dL with allopurinol ... all you are doing is retarding the rate at which the crystals will deposit," he said.

Another agent being investigated for gout is uricase, which converts uric acid to the more soluble allantoin. A commercially available formulation, rasburicase, is used for the treatment of tumor lysis syndrome. Although that drug is very effective for lowering serum urate levels, it carries a black box warning regarding anaphylaxis, Dr. Wortmann said.

Accordingly, two companies have been working on developing pegylated formulations, based on the principle that the polyethylene glycol would make uricase less antigenic and increase the half-life. Dr. Wortmann disclosed that he is also a consultant to Savient Pharmaceuticals Inc., the manufacturer of one of these formulations, Puricase.

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Fibromyalgia Diagnosis, Therapy Vary by Provider

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Rheumatologists and primary care physicians tend to use different diagnostic tests and prescribe different treatments for fibromyalgia syndrome, survey results indicated.

A large fraction of physicians in both groups did not follow the American College of Rheumatology (ACR) 1990 criteria for diagnosing fibromyalgia, Dr. Terence W. Starz and his associates reported in a poster presentation at the annual meeting of the American College of Rheumatology.

"I don't know what that means," conceded Dr. Starz, a rheumatologist at the University of Pittsburgh Medical Center. "We've got to adhere to criteria" to develop standards of care, he said in an interview.

Questionnaires e-mailed to 199 rheumatologists throughout Pennsylvania and 183 primary care physicians in the Southwestern portion of the state were returned by 74 (37%) of the rheumatologists and 89 (49%) of the primary care physicians.

Rheumatologists were significantly more likely to use ACR criteria to diagnose fibromyalgia (56, or 76%) compared with primary care physicians (50, or 56%). The two groups also differed significantly in the use of tests to measure levels of vitamin D, rheumatoid factor, antinuclear antibody, and anti-cyclic citrullinated peptide (anti-CCP) antibody. They reported similar rates of testing for thyroid function, metabolic profile, and human leukocyte antigen B27.

"We need to determine which ones

of those should be utilized, because they're very expensive," Dr. Starz said.

Vitamin D levels were ordered by 36 rheumatologists (49%) and 15 primary care physicians (17%). Tests for rheumatoid factor were ordered by 43 (58%) and 68 (76%), respectively. Rheumatologists were more likely to measure anti-CCP level (24, or 32%) than were primary care physicians (5, or 6%) but less likely to test for antinuclear antibody (45, or 61%, compared with 68, or 76%, of primary care physicians).

The two groups reported similar perceptions about the pathophysiology of fibromyalgia. Approximately three-fourths said fibromyalgia is both a medical and psychological condition, less than 20% said it's solely a medical condition, and less than 10% said it's solely a psychological condition, judging from the findings in the research, which was recognized as a "notable poster" by ACR.

Nearly all physicians in both groups prescribed exercise and physical therapy to treat fibromyalgia, but their use of most other therapies differed significantly.

Cognitive therapy was prescribed by 39 rheumatologists (52%) and 26 primary care physicians (29%). Non-steroidal anti-inflammatory drugs were prescribed by 42 (57%) of the rheumatologists and favored by primary care physicians (75, or 84%). "The data on NSAIDs, though, are not very good for fibromyalgia," Dr. Starz said.

The primary care physicians also were significantly more likely to use selective serotonin reuptake inhibitors (68, or 76%) compared with rheumatologists (42, or 57%).

The investigators reported no conflicts of interest. ■

Dual-Energy CT Imaging May Play Role in Gout Diagnosis

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Dual-energy computed tomography scans showed red-colored uric acid deposits in 20 consecutive patients with clinically obvious tophaceous gout but not in 10 control subjects with other nongout joint conditions.

The 100% sensitivity and specificity of dual-energy computed tomography (DECT) scans to identify uric acid deposits could provide a sorely needed accurate imaging tool to aid in the diagnosis of gout and its response to treatment, Dr. Abdullatif M. Alarfaj said at the annual meeting of the American College of Rheumatology.

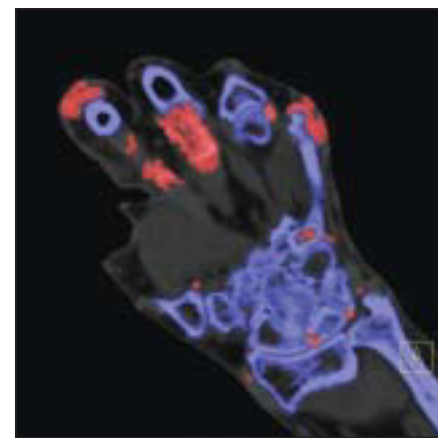
DECT assesses chemical composition and provides specific color-coded displays to differentiate between uric acid (which shows up as red), calcium (blue), and other renal calculi, previous investigators have shown.

The current proof-of-concept study, in addition to assessing the accuracy of DECT in gout patients, also measured the uric acid burden in peripheral joints and performed a computerized quantification of tophus volume. The volume of uric acid deposits in each anatomic area was measured by automated volume estimation software. The sum of tophus volume in the hands, wrists, elbows, feet, ankles, and knees comprised the total uric acid volume of peripheral joints.

DECT scans identified 440 areas of urate deposition, compared with 111 areas identified on clinical examination, reported Dr. Alarfaj of the University of British Columbia, Vancouver, and his associates. The investigators have no con-

flicts of interest related to this study.

DECT could be useful in detecting subclinical tophus deposits and the extent of intra- and extra-articular gout, Dr. Alarfaj suggested. Treatment response might be monitored by using DECT to measure both individual tophus volume and total tophus burden. ■



DECT differentiates uric acid deposits (red) and calcium in bone (blue).



The 3-D DECT image shows numerous tophi in the same patient.

IMAGES COURTESY DR. HYON CHOI