As First-Line Gout Tx, Allopurinol Is Effective, Economical

**BY MICHELE G. SULLIVAN**

**EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF PHYSICIANS**

SAN DIEGO – Allopurinol should remain the first-line agent for gout prophylaxis, despite competition from a newer drug, febuxostat, according to Dr. John Pendleton.

Allopurinol is very effective, can be safely titrated for those with renal impairment, and is the most cost-effective option, he said at the meeting.

“With either drug, the goal is to lower uric acid levels to below 6 mg/dl,” said Dr. Pendleton, referring to data from two large trials with patients treated with urate-lowering drugs.

In the study, "among the 81 patients with an uric acid level less than 6 mg/dl, 88% had no recurrent attacks during the 3-year observational period," he said.

Allopurinol has been called the "standby drug" for gouty arthritis for 60 years, and still performs admirably, he noted. Most initial doses range from 50 to 300 mg/day, but "some recent studies suggest that only 25% of patients will reach the uric acid target on that regimen. For many patients, we need to increase the dose to get that level down."

The dose should be increased every 3-4 weeks to reach the uric acid target level; doses of up to 800 mg/day are approved for this indication.

"But if you’re not able to achieve this desired level by pushing the dose close to 800 mg, I would consider trying febuxostat.

Febuxostat, a xanthine oxidase inhibitor, is more selective and potent than allopurinol in the liver and very little of the active drug is excreted renally, raising the possibility that it might be safer in patients with mild to moderate renal insufficiency," Dr. Pendleton said.

The researchers randomized patients to receive a subcutaneous injection of 150 mg canakinumab or an intramuscular injection of 40 mg trimetrexate acetamide.

Patients who reflared during the subsequent 12 weeks during the first phase of the study qualified to receive an additional dose of their assigned drug with each flare.

One of the study’s two primary end points was pain resolution at 72 hours after initial treatment. At that time, patients treated with canakinumab in the Beta-RELIEVED study had an average pain score that was 11 mm lower than that of patients in the comparator group, a statistically significant difference, reported Dr. Alexander So, a study co-investigator and professor of rheumatology at the University of Lausanne (Switzerland).

Patients who were treated with canakinumab began to show significantly better pain reduction, compared with those who got triamcinolone within 12 hours after their first dose, and the advantage in pain relief continued each time the investigators measured pain during the first 7 days after treatment, Dr. So said. Neither Dr. So nor Dr. Schlesinger reported the results for this end point from the Beta-RELIEVED II trial.

The second primary end point was the percentage of patients having new flares during the first 12 weeks following their initial therapy. In the Beta-RELIEVED trial, 19% of the 115 patients who were treated with canakinumab and 17% of the 115 patients treated with triamcinolone had a new flare, a 55% relative risk reduction with canakinumab that was statistically significant.

In the second trial, canakinumab use led to a 68% relative reduction in new flares, also a statistically significant difference in the study that randomized 226 patients, Dr. Schlesinger reported.

The canakinumab-treated patients also showed other signs of superior response in several secondary efficacy measures. Patients in the canakinumab group had a significant reduction in their mean number of flares, significantly less inflammation and swelling, and better suppression of inflammatory markers after 12 weeks, the researchers said.

In the safety analysis, canakinumab was associated with similar rates of all adverse events, a similar low rate of serious adverse events, and a similar low rate of adverse events leading to discontinuation, compared with patients who received triamcinolone.

Canakinumab Effective, Safe for Gouty Arthritis

**BY MITCHEL L. ZOLER**

**FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY**

LONDON – Use of canakinumab led to greater reductions in pain among patients with acute gouty arthritis flares after 3 days, and superior prevention of new flares during 12 weeks of follow-up, compared with triamcinolone acetoneide in a pair of phase III trials that together enrolled 456 patients.

“Canakinumab is a potential new therapeutic option for acute flares in frequently flaring gouty arthritis patients with limited treatment options,” Dr. Naomi Schlesinger said at the meeting.

Major Finding: At 3 days after a single drug dose, gouty arthritis patients who were treated with canakinumab had a statistically significant, average reduction of 11 mm on their pain score, compared with patients who were treated with triamcinolone acetoneide (on a 0- to 100-mm visual analog scale). After 12 weeks on randomized treatment, patients treated with canakinumab had a statistically significant 55%-68% relative decrease in new-flare frequency, compared with triamcinolone acetoneide-treated patients.

Data Source: The Beta-RELIEVED and Beta-RELIEVED II trials, two identically designed studies that together randomized 456 patients with recent flares of gouty arthritis who were contraindicated for, intolerant of, or unresponsive to NSAIDs and colchicine to treatment with canakinumab or triamcinolone acetoneide.

Disclosures: The beta-RELIEVED trials were sponsored by Novartis, which markets canakinumab (Ilaris). Dr. Schlesinger said that she is on the advisory board of Novartis, Enzyme Rx, Takeda, URL Pharma, and Savient. She is a consultant to and has received research grants from Novartis, and is on the speakers bureau of Takeda and Savient. Dr. So said that he is a consultant to Novartis, Bristol-Myers Squibb, Merck, Pfizer, and UCB Pharma. Dr. Khanna said that he is a consultant to Novartis, Takeda, Savient, and UCB Pharma.

Allopurinol effectively prevents gout crystals from forming in the blood, even though only 25% of patients will reach the uric acid target on that regimen, according to Dr. John Pendleton.

Allopurinol has been the “gold standard” of the comparator, he said.

The studies concluded that 40 mg of febuxostat was as effective as 300 mg of allopurinol. “The higher dose [of febuxostat 80 mg] seemed to be more effective than 400 mg allopurinol, but again, the studies did not allow for an upward titration of the comparator,” he said.

Although none of the patients in those trials had a creatinine level of more than 2.5 mg/dl, “a short-term study suggests that febuxostat dosing would not need to be adjusted even with a very low creatinine clearance [of 10-29 mL/min]. But just the same I would be very careful in that setting,” Dr. Pendleton said (Am. J. Ther. 2005;12:22-34).

Dr. Pendleton said he had no disclosures.