Got Gout? Duke Leads Study of New Treatment

September 2 2008

(PhysOrg.com) -- A new drug designed to normalize levels of uric acid in the blood appears to be safe and tolerable and may help patients with the painful arthritic condition known as gout better cope with their disease, say researchers at Duke University Medical Center.

The results of a phase II clinical trial show that the drug, an enzyme called pegloticase, lowered uric acid in blood to target levels within just a few hours in a majority of the participants.

"We were delighted to see this response, because all of the patients in our trial had already tried all the existing treatments for gout, and nothing was helping them," said John Sundy, M.D., a rheumatologist at Duke and the lead author of the study.

During treatment most of the patients continued to have gout flares and a majority developed non-neutralizing antibodies to the drug, which shortened the half-life of the drug in the bloodstreams of some patients.

The study is online and will appear in the September issue of the journal Arthritis & Rheumatism.

Often incorrectly depicted as just a disease of overindulgent old men, gout usually takes people by surprise, says Sundy. "The typical patient is a male, in his 40s or 50s, who wakes up one morning with a searing pain in one of his big toes."

Gout arises when excess uric acid builds up in the joints. Uric acid is a natural byproduct of DNA metabolism and it is normally excreted in urine. But when that process is too slow, the level of uric acid in the blood rises and the excess turns into crystals, triggering severe inflammation in joints. In some patients, that can lead to the accumulation of painful knots of crystallized uric acid that can be the size of golf balls (called tophi) that form around the joints and tendons. In extreme cases, gout can leave patients wheelchair-bound and unable to handle basic day to day tasks like cooking or buttoning clothes.

It is estimated that roughly five million people in the U.S. suffer from gout, and while most of them are men, Sundy notes that the prevalence of gout is higher than that of rheumatoid arthritis in women over age 60. Current standard of care includes the use of the drugs allopurinol and probenecid. "But about 5 percent of patients will stop allopurinol because of side effects and it is often not effective at the most commonly prescribed dose," said Sundy. "We're looking at about 50,000 people who need some new options. We haven't seen any new treatments for the underlying cause of gout in 40 years."

Pegloticase was discovered after nearly two decades of laboratory research at Duke under the direction of Michael Hershfield, M.D. Hershfield, who is not involved in the clinical study of pegloticase, says it helps get rid of excess uric acid by converting it into a substance that is more easily eliminated.

Sundy, along with colleagues in other medical centers and at Savient Pharmaceuticals, the company that is developing pegloticase, studied the use of the drug in 41 patients who were randomized to one of four treatment groups. Participants took either 4 or 8 milligrams every two weeks, or 8 or 12 milligrams every four weeks, for a 12 or 14 week period. The treatment is an infusion that takes about two hours.

Researchers found that pegloticase normalized uric acid levels within six hours for participants in all dosage groups, and those levels were sustained throughout the treatment period in the two groups at the higher dosage levels. The most effective dose was found to be 8 milligrams every two weeks.

During the treatment, 88 percent of the patients experienced gout flares, which can happen for a while when uric acid levels are lowered. Some of the patients also experienced mild to moderate side effects, including reactions to the infusion and joint pain.

"The generally accepted goal of therapy is to reduce serum urate concentrations to less than 6 milligrams per deciliter, and we found that pegloticase can do that very, very quickly," says Sundy. "Perhaps what is most important is that it did this in patients who had run out of therapeutic options."

Sundy says more studies need to be conducted to confirm and expand the findings, but says he is encouraged by the results. Results of a phase III study of pegloticase are slated for presentation of the annual meeting of the American College of Rheumatology in October.

Co-authors of the study include Michael Becker, M.D., from the University of Chicago Pritzer School of Medicine; Herbert Baraf, M.D., Arthritis and Rheumatism Associates, Wheaton, MD; Andre Barkhuisen, M.D., Oregon Health Sciences University; Larry Moreland, M.D., University of Alabama at Birmingham; and William Huang, PhD; Royce Waltrip II, M.D.; Allan Maroli, PhD; and Zeb Horowitz, M.D.; all from Savient Pharmaceuticals.

Provided by Duke University