Novel OA Pain Reliever Lowered Blood Pressure

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PARIS — Naproxcinod, an investigational pain reliever being developed for osteoarthritis, resulted in significantly lower blood pressure than did naproxen in a pivotal phase III clinical trial.

Conventional NSAIDs such as naproxen, as well as selective cyclooxygenase (COX)-2 inhibitors, are known to affect blood pressure adversely and can counteract the benefits of antihypertensive agents. This hypertensive action is thought to be an important mechanism in the increased cardiovascular risk that has led to across-the-board black box warnings for NSAIDs, Dr. Brigitte Duquesroix, director of clinical research at NicOx S.A., in Sophia Antipolis, France, noted at the annual European Congress of Rheumatology.

Naproxcinod is the first drug in a new class of anti-inflammatory analgesics known as COX-inhibiting nitric oxide donators. It has two mechanisms of action: inhibition of both COX-1 and -2 via metabolism to naproxen, plus sustained release of nitric oxide. The latter is known to have multiple beneficial cardiovascular effects, including maintenance of vascular endothelial function, antiplatelet activity, and modulation of smooth muscle cell proliferation. It also may have a protective effect in the GI tract.

Dr. Duquesroix reported on 918 patients with knee osteoarthritis seen at 110 U.S. sites. They were randomized in a double-blind fashion to 13 weeks of naproxcinod at 375 or 750 mg b.i.d., naproxen 500 mg b.i.d., or placebo. Half of the participants were hypertensive at baseline. Office blood pressure readings were obtained 2-4 hours after the morning dose.

Over the full 13 weeks, both doses of naproxcinod resulted in lower systolic and diastolic blood pressures, compared with baseline readings and with naproxen. At week 13, the naproxcinod 750-mg b.i.d. group had a mean 2.9–mm Hg lower systolic and 1.8–mm Hg lower diastolic blood pressure, compared with the naproxen 500-mg b.i.d. group. Patients on naproxcinod at 375 mg b.i.d. averaged a 1.8–mm Hg lower systolic and 1.6–mm Hg lower diastolic blood pressure than did naproxen-treated patients.

Analgesic efficacy of naproxcinod at both doses was superior to placebo and comparable with naproxen. GI adverse events were noted in 17% of patients on 750-mg b.i.d. dose, 13% on the lower dose of naproxcinod, 24% of those on naproxen 500-mg b.i.d. dose, and 12% on placebo.

Two additional confirmatory pivotal phase III trials are ongoing.

NicOx plans to file for U.S. marketing approval for naproxcinod next year, Dr. Duquesroix said in an interview. ■

Use X-Rays Plus Scintigraphy to Assess Knee OA

SAN FRANCISCO — Traditional radiographic assessment of osteoarthritis in the medial compartment of the knee should be combined with scintigraphic data for the most accurate evaluation, according to a poster presentation at the annual meeting of the American Academy of Orthopaedic Surgeons.

By providing information on the metabolic activity of bone, scintigraphy enables degenerative changes in the knee to be detected early, before joint disease shows up in x-rays, said Dr. Scott F. Dye of the orthopedic surgery department at the University of California, San Francisco.

An anterior-posterior technetium bone scan provides a window into the metabolic activity of living bone, according to Dr. Dye and his associates. Knees can be metabolically worse or better than the x-ray results suggest. Combining the structural (x-ray) and metabolic (scintigraphy) studies provides a better assessment of the status of the knee and response to therapies.

The earliest stages of medial compartment osteoarthritis of the knee often are secondary to meniscal tears, and 80% of patients with medial meniscus tears will show loss of osseous homeostasis on scintigraphy despite normal x-ray results. This allows for identification of joints at risk of degenerative disease "at a time when the process can be fully reversed," said Dr. Dye, who has no association with companies that make scintigraphic equipment.

—Sherry Boschert