13-country precision trial looks at cardiovascular effects of anti-inflammatory drug use

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A 10-year trial involving osteoarthritis and rheumatoid arthritis patients in 13 countries reveals new insights on the cardiovascular safety of widely used nonsteroidal anti-inflammatory drugs and COX-2-specific inhibitors, according to new research findings to be presented on this week at the 2016 ACR/ARHP Annual Meeting.

Osteoarthritis, or OA, is the most common joint disease affecting middle-age and older people. It is characterized by progressive damage to the joint cartilage—the cushioning material at the end of long bones—and causes changes in the structures around the joint. Rheumatoid arthritis (RA) is a chronic disease that causes pain, stiffness, swelling, and limitation in the motion and function of multiple joints. Though joints are the principal body parts affected by RA, inflammation can develop in other organs as well.

Chronic use of non-selective, nonsteroidal anti-inflammatory drugs (NSAIDs) and selective COX-2 NSAIDs (such as celecoxib) is widespread among OA and RA patients, although these diseases have an associated risk of cardiovascular disease (CVD). The relative cardiovascular safety of these drugs remains unclear. So a group of researchers, led by Cleveland Clinic Coordinating Center for Clinical Research, in collaboration with colleagues at Brigham and Women's Hospital, conducted the PRECISION trial - a very large randomized controlled trial (RCT) - to directly and prospectively compare the CV

safety of these anti-inflammatory agents.

"The results of the PRECISION trial offer clinicians increased detail on how to monitor patients who take chronic NSAIDs with a more individualistic approach," says Elaine Husni, M.D., MPH says M. Elaine Husni, MD, MPH; vice chair, Department of rheumatic and immunologic diseases; director, Arthritis Center, Orthopedic and Rheumatologic Institute; Cleveland Clinic.

"The PRECISION Trial provides critical information for patients and their providers about the safe use of commonly used analgesics, including celecoxib, ibuprofen and naproxen," says Daniel Solomon, MD, MPH, chief, Section of Clinical Sciences, Division of Rheumatology and Division of Pharmacoepidemiology at Brigham and Women's Hospital. "The analyses presented at the ACR focusing on osteoarthritis and rheumatoid arthritis add even more precise information allowing providers to tailor analgesic recommendations for patients. The PRECISION Trial has taught us that there is tremendous nuance to the comparative safety of these agents."

There is an ongoing debate over the benefits and risks of using non-steroidal anti-inflammatory drugs for patients with OA and RA. Studies have demonstrated adverse cardiovascular outcomes which resulted in the withdrawal of the selective COX-2 inhibitor rofecoxib in 2004. This led the U.S. Food and Drug Administration (FDA) to mandate a cardiovascular safety trial for the remaining selective COX-2 inhibitor, celecoxib. The Prospective Randomized Evaluation of Celecoxib Integrated Safety versus Ibuprofen or Naproxen (PRECISION) trial sought to determine whether celecoxib shares the same CV toxicity observed in the rofecoxib trials using a non-inferiority trial design.

PRECISION was a double-blind, triple-dummy RCT conducted in 13 countries over 10 years, including 24,081 patients in 923 study sites.

Eighty percent of the participants came from the United States. Subjects were required to have a known history of CV events, such as myocardial infarction, stroke or coronary re-vascularization, or evidence of CV risk based on traditional risk factors. Participants also were required to have a physician diagnosis of OA or RA, daily need for NSAID therapy, no CV events within the last 90 days and no contraindications to the use of these agents.

Ninety percent of the enrolled patients in the trial and final analyses had OA, and 10 percent had RA. The mean age of participants with OA was 64 years and with RA was 61 years. Of the OA subjects, 63 percent were female. Of the RA subjects, 73 percent were female. Age and gender distribution did not differ by NSAID treatment assignment. Adherence was 80 percent over at least six months of follow-up, with a median follow-up of 18 months. Cardiovascular (CV), gastrointestinal (GI), renal adverse events, and all-cause mortality were analyzed for both subjects with OA and RA by treatment arms.

Subjects were randomized to receive 100-200 mg of celecoxib twice a day, 600-800 mg of ibuprofen three times a day, or 375-500 mg of naproxen twice a day. All subjects were provided with open-label esomeprazole at a dose of 20-40 mg once a day, and aspirin was allowed as part of standard of care if applicable.

For the results of the PRECISION trial, please attend the late-breaking clinical trial presentation on November 15th 4:30 p.m. ET.

Provided by American College of Rheumatology

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