



Arthritis News

Media Contact: Tammy McCoy
(404) 633-3777 (until Oct. 15)
(210) 582-7010 (Oct. 16–Oct. 21)
tmccoy@rheumatology.org

**Embargoed for Release at
6:15 PM ET, Sunday Oct. 17, 2004**

PPI TREATMENT PRESCRIPTION LEVELS NOT IMPACTED BY COX-2 THERAPY

SAN ANTONIO, TEXAS—Surprisingly, the use of COX-2 therapy does not decrease the number of prescriptions written for ulcer prevention medications such as proton pump inhibitors (PPIs) in patients with rheumatoid arthritis and osteoarthritis, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Common generic and prescription NSAIDs (non-steroidal anti-inflammatory drugs) decrease cyclooxygenase enzymes 1 and 2 (COX 1 and COX 2). Because cyclooxygenase 1 is important in protecting the stomach against ulcers, patients on NSAID therapy can experience side effects including gastrointestinal symptoms and ulcers. As a result, patients taking these NSAIDs may require additional medications such as proton pump inhibitors—a class of medications that protect against these stomach side effects. Because COX-2 therapies inhibit only cyclooxygenase 2, the enzyme responsible for inflammation and pain, and not COX 1, they are less likely to cause ulcers. So, while Cox-2 NSAIDs are more expensive than traditional NSAIDs, their use has been justified on the assumption they would decrease the number of prescriptions for medications to prevent traditional NSAIDs side effects.

To evaluate this assumption, researchers conducted a three-year, semi-annual evaluation on 10,392 rheumatoid arthritis and osteoarthritis patients who had not received prior PPI therapy. The annual rate of starting a PPI for those on COX-2 was 9.8% compared to 6.7% for those on traditional NSAIDs, a rate difference of 3.1%. A history of gastrointestinal ulcers were the strongest predictor of prescriptions for PPIs, followed by epigastric pain, heartburn and low dose aspirin. Adjusting for baseline differences in severity and GI history, researchers determined patients were as apt to receive COX-2 therapy as a traditional NSAID.

“What we found is that, in real life, people who take COX-2s receive PPIs at the same rate as do people on traditional therapies,” said Frederick Wolfe, MD, National Data Bank for Rheumatic Diseases, Wichita, Kansas, and an investigator in the study. “Therefore, there is no reduction in PPI prescriptions that can be attributed to COX-2 therapy in the patients with arthritis in this study.”

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR’s annual meeting, see www.rheumatology.org/annual.

###

Editor’s Notes: Dr. Wolfe will present this research during a scientific session at the ACR Annual Scientific Meeting from 12:15–2:00 PM CT (1:15–3:00 PM ET) on Wednesday, October 20, Exhibit Hall C–D of the Henry B. González Convention Center.

Publishing Title: Factors Related to Proton Pump Inhibitor (PPI) Prescription: COX-2 Therapy Does Not Reduce the Rate of PPI Prescription

Frederick Wolfe¹, Elizabeth Benito Garcia², Kaleb Michaud¹. ¹National Data Bank for Rheumatic Diseases, Wichita, KS; ²Brigham and Women's Hospital, Boston, MA

PURPOSE: Proton pump inhibitors (PPI) are widely-used, effective drugs for the treatment and prophylaxis of GI symptoms and ulcers. COX-2 specific NSAIDs (COX-2) reduce ulcer rates and dyspeptic symptoms in arthritis patients compared with users of non-specific NSAIDs (NSAID) in clinical trials. A hypothesized benefit of COX-2 therapy is the reduced need for PPI treatment. We investigate the extent to which RA features, demographics and COX-2 and NSAID are associated with prescription of PPI in order to define the contribution of COX-2 and NSAID to PPI prescription.

METHODS: Using a longitudinal data bank, we evaluated 10,392 RA and OA patients who were not receiving PPI therapy at their first assessment. Patients were assessed semiannually over a 3 years period. To adjust for non-random COX-2 prescription we developed a propensity score from 19 demographic, treatment, GI and arthritis severity variables. Data were analyzed initially using time-varying COX proportional Hazards regression, but without propensity score control (Table 1), and then after adjustment for age sex and propensity score.

RESULTS: Among patients receiving COX-2 therapy the annual incidence of starting a PPI was 9.8% compared to 6.7% for those on NSAID, A rate difference of 3.1% (95% C.I.: 2.0 to 4.1). Table 1 describes the age and sex adjusted time-varying predictors of PPI prescription. The most powerful predictor was development of a GI ulcer (hazard ratio (HR) 5.1) followed by baseline GI history (HR 2.1). Other important predictors were epigastric pain (HR 1.8), heartburn (HR 1.7) and low dose aspirin (HR1.3). NSAID was not associated with PPI use (p = .424), but COX-2 was significantly associated with prescription (HR 1.2). These data represent risk factors in actual practice. However, because of non-random prescription and channeling bias, they do not represent a causal model for treatment variables.

To ascertain the causal relationship between COX-2 and PPI prescription we used a baseline propensity score for the risk of COX-2 prescription. Adjusted for the risk of COX-2 prescription, the HR for COX-2 was 1.0, p = 0.688.

CONCLUSIONS: Although the time-varying COX models for PPI use suggest an increased use of PPI by patients receiving COX-2, this effect is related to non-random prescription; and the propensity score adjusted COX-2 HR is 1.0. Therefore use of COX-2 therapy does not alter the risk of PPI prescription and no economic benefit related to reduced PPI prescription can be attributed to COX-2 therapy.

Risk of PPI Prescription

Variable	HR	P-value	95% C.I.
COX-2	1.2	0.002	1.1 to 1.4
NSAID	0.9	0.424	0.8 to 1.1
ASA (low dose)	1.3	<0.000	1.1 to 1.4
HAQ	1.2	<0.000	1.1 to 1.3
Epigastric pain	1.8	<0.001	1.5 to 2.8
Heartburn	1.7	<0.001	1.5 to 2.0
Ulcer	5.1	<0.001	4.0 to 6.4
Baseline GI Risk	2.1	<0.001	1.8 to 2.4

Author Disclosure Block: F. Wolfe, TAP Pharmaceuticals 2; E. Benito Garcia, None; K. Michaud, None.

Author disclosure legend—Authors' disclosures of third-party relationships are listed in numeric format according to the following listing:

None—Nothing to disclose; 1—Stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2—Research grants; 3—Employment (full or part-time); 4—Ownership or partnership; 5—Consulting fees or other remuneration (payment); 6—Non-remunerative positions of influence such as officer, board member, trustee or public spokesperson; 7—Receipt of royalties; 8—Speakers bureau.