



57th Annual Scientific Session
MARCH 29 – APRIL 1 • CHICAGO

EMBARGOED FOR RELEASE
Monday, March 31, 2008
10:00 a.m. CDT

CONTACT: Andrew Crosby
(901) 575-0010
acrosby@crosbyvolmer.com
Amy Murphy
(202) 375-6476
amurphy@acc.org
ACC.08 Newsroom:
(312) 949-3450

CARDIOVASCULAR RISK DIFFERS BY CELECOXIB DOSE

New Findings May Help Guide Treatment Decisions for Patients who Benefit from Selective Cox-2 Inhibition

CHICAGO, IL – Research presented today at the American College of Cardiology’s 57th Annual Scientific Session suggests that physicians should prescribe the lowest doses of Celecoxib possible, especially in higher risk patients. Results of this trial showed evidence of dose and regimen differences in risk, as well as evidence of an interaction between baseline cardiovascular risk and Celecoxib dose, and suggest that the adverse effect of dose is most pronounced in higher risk patients.

Since Celecoxib, which currently carries an FDA-mandated black box warning, remains the only coxib available in the United States, and is the most commonly used cox-2 inhibitor in the world, the findings from this patient-level pooled analysis of adjudicated data (“The Cross Trials Safety Assessment”) have important implications for treating patients who benefit from coxibs.

Previous observational studies and randomized trials have reported increased cardiovascular risk associated with cyclooxygenase-2 (cox-2) inhibitors (coxibs). To assess the relationship between baseline cardiovascular risk and the effect of Celecoxib on cardiovascular events, the National Cancer Institute (NCI) commissioned and funded a meta-analysis of six randomized trials comparing Celecoxib to placebo.

To better understand the cardiovascular risk profile associated with long-term use of Celecoxib, the NCI asked investigators of trials with a planned follow-up of three or more years to submit their data for central adjudication and combine their analyses with the data from the Adenoma Prevention with Celecoxib (APC) and the Prevention of Sporadic Adenomatous Polyps (PreSAP) studies.

- more -

This study combined results from six trials comparing Celecoxib to placebo for conditions other than arthritis with a planned follow-up of three years; 7,950 patients were administered Celecoxib in one of three dose regimens (400mg once a day, 200mg twice a day, or 400mg twice a day).

With 16,070 patient-years of follow-up, the researchers calculated a hazard ratio for all dose-regimens combined and individual hazard ratios for each dose regimen, and examined whether Celecoxib-related risk was associated with baseline cardiovascular risk. A modified Framingham cardiovascular risk score was used to assign cardiovascular risk for each patient. All cardiovascular endpoints were adjudicated from source documents, with the primary endpoint being the combination of cardiovascular death, myocardial infarction, stroke, heart failure or thromboembolic event.

The hazard ratio for the composite endpoint combining the tested doses was 1.6. The risk was lowest for the 400mg daily dose (hazard ratio 1.1), intermediate for the 200mg twice daily dose (with nearly a two-fold risk of adverse cardiovascular events), and highest for the 400mg twice daily dose (with approximately a three-fold risk of adverse cardiovascular events). Celecoxib was associated with increased risk regardless of baseline aspirin use.

The Celecoxib Cross-Trials Safety Analysis provides the most comprehensive placebo-controlled assessment of cardiovascular risk of Celecoxib for the doses tested.

“By adding the results of four additional trials to the previously reported APC and PreSAP trials, this analysis had the power to address dose and regimen differences and the interaction between baseline cardiovascular risk and the risk associated with Celecoxib,” said Scott D. Solomon, M.D., Director, Noninvasive Cardiology, Brigham and Women’s Hospital, and lead investigator of the NCI-sponsored study.

“These data should provide some measure of comfort in prescribing Celecoxib to patients with very low cardiovascular risk,” added Dr. Solomon, “Similarly, we should be cautious in prescribing Celecoxib to patients who have elevated baseline cardiovascular risk. While the doses tested were generally higher than those prescribed for the majority of arthritis patients who take Celecoxib, and we do not have direct data on the cardiovascular risk associated with lower doses, our data support the recent American Heart Association scientific position statement suggesting that physicians should prescribe the lowest doses of Celecoxib possible, especially in higher risk patients.”

The study will be simultaneously published in the online version of *Circulation*.

Dr. Solomon will present this study, “Cardiovascular Risk of Celecoxib in Six Randomized Placebo-Controlled Trials: The Cross-Trials Safety Assessment Pooled Analysis” on Monday, March 31 at 11:15 a.m. in North Hall B1.

###

The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines- and to influence health care policy. ACC.08 is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.