Celecoxib Reduced Lung Lesion Biomarker Levels

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CHICAGO — Short-term treatment with high-dose celecoxib reduced expression levels for a biomarker associated with precancerous lung lesions in a chemoprevention study of about 200 current and former smokers, according to data presented at the annual meeting of the American Society of Clinical Oncology.

The randomized, double-blind prospective study found a significant reduction in Ki-67 expression, as well as reduced levels of cyclooxygenase-2 (COX-2) in patients who received 400 mg twice daily of celecoxib (Celebrex) for 3 months.

"We cannot sit here and say that taking celecoxib is going to prevent lung cancer. That needs further, larger-scale studies," Dr. Edward S. Kim, the lead author and a medical oncologist at the University of Texas M.D. Anderson Cancer Center, Houston, cautioned at a press briefing at the ASCO annual meeting.

Between November 2001 and September 2006, the researchers enrolled 212 current and former smokers with at least a 20 pack-year smoking history. Most patients did not have a prior cancer, but those who did had been disease free for 6 months. The median age of the study participants was 53 years. The study was funded by a grant from the National Cancer Institute, part of the National Institutes of Health.

Study participants were randomized into four treatment arms: 3 months of placebo, then 3 months of celecoxib; 3 months of celecoxib, then 3 months of placebo; 6 months of celecoxib; or 6 months of placebo. Celecoxib was administered at 200 mg twice daily, and then increased to 400 mg twice daily.

In addition, patients underwent three consecutive bronchoscopies: at study enrollment, at 3 months, and at 6 months. Predetermined biopsies were also performed at the same time.

The primary end point of the study was change in the Ki-67 marker (a nuclear protein that appears to be related to cell proliferation) from baseline to 3 months. Over a 3-month period, high-dose celecoxib, when compared with placebo, did reduce the expression levels of Ki-67 for patients who received 400 mg of celecoxib twice daily. The effect was not seen in the 200-mg dose. The study was designed to detect a 1.2% difference in Ki-67 between celecoxib and placebo with a two-sided 5% level of significance.

In addition, the researchers looked at two other biomarkers: COX-2 and NF-kappaB. The COX-2 levels showed a significant decrease with celecoxib treatment at 400 mg, and decreases were close to significant with the 200-mg dose. Levels of NF-kappaB were significantly lowered with the 400-mg dose of celecoxib for former smokers only.

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"We cannot ... say that taking celecoxib is going to prevent lung cancer." That needs more studies, said Dr. Edward S. Kim.

The study does show the safety and tolerability of celecoxib, Dr. Kim said. Three study participants experienced one grade 3 toxicity, but the researchers observed no cardiac toxicities. The study also showed that it was safe for patients to undergo consecutive bronchoscopies, he said.

When the researchers first decided to study celecoxib, prior to the 2001 launch of the study, cardiac safety concerns had yet to be raised about COX-2 inhibitors, Dr. Kim said. In December 2004, officials at the M.D. Anderson Cancer Center voluntarily suspended the trial at the request of the National Cancer Institute and Pfizer Inc., which markets Celebrex.

The study reopened in May 2005 after officials at the Food and Drug Administration recommended that Celebrex continue to be evaluated for cancer treatment and prevention. ■