Common Painkillers Help Prevent Bladder Cancer Recurrence

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Conclusion: "There is an increased frequency of cyclooxygenase-2 expression in patients with high-grade invasive bladder cancer. Also, patients with stage T1G3 bladder cancers who overexpress COX-2 have an increased risk of recurrence and progression." American Urological Association, 2002, Presented by H. Barton Grossman, MD, University of Texas M.D. Anderson Cancer Center, Houston.

Trial info -click here

{/niftybox}On this page: Cox-2 Inhibitors Update May 2005: Risks with Cox-2 inhibitor use; August, 2007:Non-Steroidal anti-inflammatories/NSAIDs (aspirin)

A number of cancers appear to overexpress the COX-2 enzyme, which may play several roles in the development of cancer.

During the 2003 annual meeting of the American Society of Clinical Oncology, Dr. Jacques LeLorier presented new findings which showed that the use of Cox-2 inhibitors (Celebrex, Vioxx) lowers the risk of recurrence for those with superficial bladder cancer. The study also looked at results from the use of the more common, over the counter non-steroidal anti-inflammatories (called NSAIDs for short)), such as aspirin, ibuprofen, Advil, Motrin and naproxen sodium (Aleve), and found that these drugs also reduced the risk of recurrence.

61.5% of non-users had a recurrence the first year, as did 56.7% of those who used acetaminophen (Tylenol, Paracetomal). In contrast, those treated with Cox-2 inhibitors experienced 31% recurrence, and those using NSAIDs 32%.

What are the COX enzymes?

The COX enzymes produce prostaglandins, fatty acids that perform a number of hormone-like tasks. Prostaglandins alter the activities of the cells near and around where they are made. They also cause inflammation and can regulate blood flow to some organs, transport across cell membranes, and transmissions between neurons. COX-1 is responsible for the "day-to-day" production of prostaglandins, while COX-2 is highly regulated by numerous other cellular signals when needed.

Drugs which selectively target COX-2, such as Pharmacia/Pfizer's Celebrex and Bextra and Merck's Vioxx*, have attracted much attention. They have been remarkably successful, based on claims that they relieve pain and inflammation while lessening the risk of stomach ulceration and bleeding associated with traditional NSAIDs. One issue of controversy has been whether the benefit of COX-2 inhibitors in the stomach is offset by an increased risk of heart attack.

*Vioxx has since been taken off of the market due to deaths from its side effects.

Phase II and III clinical trials are now in progress studying celecoxib (Celebrex). Those qualifying for the trials must have good kidney function. For Celebrex's user profile and side effect warnings, see the FDA s page.

The NCI's Clinical Trials for bladder cancer-reducing the risk of recurrence with celecoxib:

Celecoxib in Treating Patients With Bladder Cancer- This study is currently recruiting patients.

Sponsored by M.D. Anderson Cancer Center, National Cancer Institute (NCI)

RATIONALE: Chemoprevention therapy is the use of certain drugs to try to prevent the development or recurrence of cancer. The use of celecoxib may be an effective way to prevent the recurrence of bladder cancer.

PURPOSE: Randomized phase II/III trial to study the effectiveness of celecoxib in preventing disease recurrence in patients who have bladder cancer.

Official Title: Phase IIB/III Randomized Chemoprevention Study of Celecoxib in Patients With Superficial Transitional Cell Carcinoma of the Bladder At High Risk For Recurrence

OBJECTIVES:

" Compare the time to recurrence after treatment with celecoxib vs placebo in patients with superficial transitional cell carcinoma of the bladder at high risk for recurrence.

" Correlate the modulation of one or more biomarkers with recurrence of bladder cancer and confirm the value of the marker(s) as a surrogate endpoint biomarker for bladder cancer and celecoxib.

" Determine the toxicity of celecoxib in these patients.

" Compare the quality of life of patients treated with these 2 regimens.

OUTLINE: This is a randomized, double-blind, placebo-controlled, multicenter study. Patients are stratified according to center and presence of Tis disease (yes vs no). Patients are randomized to one of two arms.

" Arm I: Patients receive oral celecoxib twice a day.

" Arm II: Patients receive oral placebo twice a day. Treatment continues on both arms for 1-2 years in the absence of unacceptable toxicity, development of recurrent or invasive bladder carcinoma, or development of a second malignancy requiring radiotherapy or systemic therapy.

click here
for more info about the trials

Update: Risks

From the National Institutes of Health:

NIH
Halts Use of COX-2 Inhibitor in Large Cancer Prevention Trial

article excerpt:

The National Institutes of Health (NIH) announced in December 2004 that it suspended the use of COX-2 inhibitor celecoxib (Celebrex" Pfizer, Inc.) for all participants in a large colorectal cancer prevention clinical trial conducted by the National Cancer Institute (NCI). The study was stopped when it was discovered that participants showed a 2.5-fold increased risk of major fatal and non-fatal cardiovascular events compared to those on a placebo.

Another study showed that the COX-2 inhibitor rofecoxib (Vioxx") caused a two-fold increased risk of cardiovascular toxicities in a trial to prevent adenomas.

"Data from the report on rofecoxib (Vioxx) informed us of the need to focus on specific cardiovascular issues, and our Institutes brought in the experts to do so", said Elias A. Zerhouni, M.D., NIH Director. "The rigor of our clinical trials system has allowed us to find this problem," said NCI Director Andrew C. von Eschenbach, M.D. NIH sponsors over 40 studies using celecoxib for the prevention and treatment of cancer [including superficial bladder cancer], dementia and other diseases. In light of these new findings, NIH Director Zerhouni requested various safety measures including a full review of all NIH-supported studies involving this class of drug.

From the National Cancer Institute:

The National Cancer Institute will notify all of the principal investigators of its sponsored trials involving COX-2 inhibitors. They will be instructed to notify their institutional review boards, data safety monitoring boards, and participants about this new information. NCI will also require that the informed consent for these trials be revised to reflect this new information and that individuals in the trials be re-consented (asked to sign new consent forms with updated information about risks and benefits of the trials).

For more information about cancer, please visit the NCI Web site at http://www.cancer.gov or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

For more information about regulation of COX-2 inhibitors by the FDA, please visit the FDA Web site at http://www.fda.gov/cder/drug/default.htm.

Non-steroidal anit-inflammatory drugs

Regular use of non-steroidal anti-inflammatory drugs (NSAIDs), especially aspirin, may decrease the risk of bladder cancer, particularly more advanced, high-grade tumors containing alterations in the tumor suppressor protein TP53, results of a study suggest.

For their study, Dr. Margaret R. Karagas of Dartmouth Medical School, Hanover, New Hampshire, and colleagues assessed lifetime use of analgesics and NSAIDs with the bladder cancer incidence in a population-based case-control study. Other common NSAIDs include naproxen (Aleve) and ibuprofen (Motrin).

Regular use of any NSAID was associated with a statistically significant reduced risk of bladder cancer, an association

that was largely due to regular aspirin use. Regular NSAID use seemed to protect against invasive, high-grade and TP53-positive tumors, in particular.

Karagas and colleagues suggest that, "in light of the chemopreventive effects of NSAIDs including aspirin for other neoplasms, the possibility that they may reduce bladder cancer incidence warrants further consideration. Studies assessing the effect on bladder cancer prognosis are lacking but would be of great interest."

SOURCE: BMC Urology, August 10, 2007. Reuters News

The complete study is available through open access here: http://www.biomedcentral.com/1471-2490/7/13

Research article Analgesic and anti-inflammatory drug use and risk of bladder cancer: a population based case control study

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