COX-2 Comeback?

By ACSH Staff — April 12, 2006

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The class of drugs known as COX-2 inhibitors took another hit with the latest liability verdict against Merck’s Vioxx from a New Jersey jury (not to mention an additional $9 million in punitive damages against the company coming yesterday). Yet despite another damage award, these drugs still offer significant, largely unrecognized potential for benefit to our health -- and not just for their originally-approved use, which is pain relief for arthritis sufferers (with a lower risk of stomach irritation than older drugs).

Scientific reports presented at American Association for Cancer Research (AACR) meetings in DC last week demonstrated that Celebrex also reduces the risk of pre-malignant colorectal polyps in patients at high risk.

Two large multi-center studies, comprising thousands of patients, yielded quite similar outcomes: both moderate and high doses of Celebrex reduced the number and size of colorectal polyps in patients selected because they previously had polyps and/or cancer of the colon. The reduction in polyps varied from 33% at a lower dose (400 mg daily) to a 45% reduction on a higher dose (800 mg daily) of the active drug (these doses are greater than those ordinarily prescribed to those suffering from arthritis pain). The higher-risk patients had a greater risk reduction.

True, the studies gave further evidence that Celebrex can increase cardiovascular (CV) problems, but while the relative risk of CV events is increased by Celebrex, the actual incidence of heart problems, the absolute risk, remains quite small. Encouragingly, gastrointestinal problems were similar in the group on the active drug and those in the placebo arm -- confirming again the relative GI safety of Celebrex, its major benefit compared to the older painkillers called NSAIDs (e.g., ibuprofen/Motrin and naproxen/Alleve).

Halting Research Out of Fear

Many similar studies on the potential beneficial effects of COX-2 inhibitors -- Celebrex, Vioxx, and Bextra -- were underway in 2004 when a Merck study on colorectal polyp prevention revealed that Vioxx raised CV risk and the drug was precipitously pulled off the market. (Ironically, that same study showed that Vioxx did indeed reduce the incidence of polyps.) The other studies on cancer chemoprevention, many sponsored by the National Cancer Institute, were halted midstream, out of fear of both adverse effects and adverse publicity. Political pressure on the Food and Drug Administration about "unsafe" drugs escalated, leading to calls for ever more stringent regulation and drug-oversight boards. Whistle-blowers and "consumer advocates" emerged from every nook and cranny, calling for drug recalls and hearings. Subsequently, an FDA panel actually supported the continued availability of Vioxx and Celebrex -- though Vioxx stayed withdrawn. Further, other studies indicated that even the older NSAIDs might increase CV risk, and this possibility is now
being addressed with controlled trials. When the smoke cleared and cooler, wiser heads prevailed, the two colorectal polyp studies presented at AACR were resumed.

What does the future hold for cancer prevention utilizing this now-suspect class of drugs? Not only colon cancer but cancers of several other sites, especially breast cancer, were being intensively studied when the Vioxx recall chilled the field.

Dr. Banu Arun of the M.D. Anderson Cancer Center in Houston was conducting a trial using Celebrex as a possible breast cancer prevention agent for high-risk women when her trial was suspended during the Vioxx hysteria. After the FDA panel allowed Celebrex to remain on the market in April of 2005, her trial was resumed, with new guidelines for study patients' CV screening and informed consent. Her reaction to the CV risk of cancer prevention drugs? "Any drug we test for the treatment or prevention of cancer has some side effects. There is no medication that doesn't. The issue is informing patients about potential side effects and selecting the best high-risk population who would have the maximum benefit and for whom the toxicity is acceptable."

While the CV risks of COX-2 drugs like Celebrex warrant serious attention, the FDA should let doctors and patients discuss appropriate options and decide on the best course of treatment. Patients with life-threatening illness or serious concerns (such as high risk for cancer, or progressive multiple sclerosis) should be able to choose to be treated with a "risky" drug, accepting the trade-off of an increased CV risk for the goal of ameliorating cancer risk. All drugs have some risk -- this decision needs to be an individual one.

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