Aspirin could be used to prevent cancer

Owen Dyer *London*

Three recently published studies indicate that aspirin, already enjoying a second lease of life in the prevention of heart disease, may soon become a first line of defence against cancer.

Two prospective, placebo controlled studies published in the *New England Journal of Medicine* (2002;348:883-90 and 891-9) looked at patients at risk of colorectal cancer. Both studies found a clear benefit from aspirin in reducing the frequency of new colorectal polyps.

The second of these studies, led by John Baron of Dartmouth Medical School, Hanover, New Hampshire, followed 1084 patients with a history of polyps and examined the patients by colonoscopy about three years after their entry into the study. The patients were split into three arms: a placebo group, a low dose group taking 81 mg aspirin daily, and a group taking 325 mg daily.

Most of the benefit was in the low dose group. The unadjusted risk ratios for new polyps were 0.81 in the low dose group (95% confidence interval, 0.69 to 0.96)

and 0.96 in the high dose group (0.81 to 1.13).

When only large or malignant polyps were considered, however, the benefits were clearer—risk ratios of 0.59 (0.38 to 0.92) in the low dose group and 0.83 in the high dose group (0.55 to 1.23).

The other study of colorectal cancer, led by Professor Richard Schilsky of the University of Chicago, followed 517 patients with previous malignant disease, dividing them into placebo and 325 mg treatment groups. Although this study lasted only a year, the researchers found a risk ratio for new polyps of 0.65 (0.46 to 0.91) in the treatment group.

Dr Cristina Bosetti of the Mario Negri pharmacological research institute in Milan, who led the Italian research, speculated at a press conference that aspirin's inhibition of the inflammatory enzyme cyclo-oxygenase-2 is the key to the drug's apparent protective effect. "The effect of aspirin can also be seen in other cancers, because cyclo-oxygenase is also implicated in cancer of the stomach and breast cancer. If this

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Aspirin could reduce incidence of colorectal polyps

is the mechanism of action the effect of aspirin could be similar for these cancers," she said.

Meanwhile an Italian study published in the *British Journal of Cancer* (2003;88:672-4) found that long term use of aspirin dramatically reduced the incidence of tumours of the mouth, throat, and oesophagus. The research pooled data from three smaller

studies to create a patient base of 965 cancer patients and 1779 controls. After controlling for factors such as smoking and diet, the researchers found that the incidence of the three types of cancer in people who had taken aspirin regularly for at least five years was a third that in people who had not taken aspirin (odds ratio 0.33 (0.13 to 0.82)). □

FDA officials argue over safety of new arthritis drug

Ray Moynihan *Washington, DC*

An external advisory panel to the US Food and Drug Administration last week rejected calls from FDA safety experts to withdraw a drug for rheumatoid arthritis from the market.

The Arthritis Advisory Committee found that the benefits of the Aventis drug leflunomide (Arava) outweighed its rare side effects, despite an internal FDA report that said that one in 200 users may be at risk of serious acute liver injury.

The report from the FDA's Office of Drug Safety, written by Dr Renan Bonnel and Dr David Graham for the advisory committee's meeting, found that there was "an absence of documented long-term benefit based on objective indices of functional ability/disability or delayed mortality."

It concluded that the "risks of leflunomide greatly exceeded its benefits." Because there were safer and effective alterna-

tives on the market, the authors recommended the drug be immediately withdrawn.

That recommendation was, however, directly contradicted by senior FDA officials, including the director of the Office of Drug Safety, Dr Victor Raczowski. He argued that many of the reports linking the drug with acute liver injury were "confounded, inconclusive, or incomplete."

The latest internal conflict comes at a time when the FDA stands accused by consumer groups of paying too little attention to drug safety. These critics include the Washington based consumer group Public Citizen, which last year petitioned the

FDA to withdraw leflunomide from the market.

Another senior FDA officer, Dr Lawrence Goldkind, told the advisory panel that an exhaustive review of data, including large health insurance databases covering more than 50 000 patients, indicated that serious liver injury was a very rare side effect of the arthritis drug.

He said that there was "no consistent pattern" of toxicity, as seen with other drugs, such as troglitazone (Romezin)—the diabetes drug withdrawn from the market in 2000. □

The reports can be viewed at www.fda.gov/ohrms/dockets/ac/03/briefing/3930b2.htm