Anti-gout drug may decrease risk for colorectal adenoma progression

November 8 2010

Allopurinol, a relatively inexpensive anti-gout medication that has been on the market for more than 20 years, may have some activity against colorectal adenomas, according to data presented at the Ninth Annual AACR Frontiers in Cancer Prevention Research Conference, held here Nov. 7-10, 2010.

Specifically, the presence of a colorectal tumor tissue biomarker, Ki67, was markedly decreased in the preliminary results of a study of patients with colorectal polyps assigned to take allopurinol.

"Allopurinol has a well-known and good safety profile, and a cost of approximately one euro for one month of treatment," said Andrea De Censi, M.D., director, medical oncology unit, Galliera Hospital, Genoa, and advisor, division of cancer prevention and genetics, EIO, Milan, Italy.

"In the era of very expensive target-therapy in oncology, it is important to search for cheap agents that could be active in cancer prevention and thus have huge public health implications,"
he said.

In colorectal tumor tissue there are high levels of ROM, or reactive oxygen metabolites.

"These ROMs are thought to be important for development of tumor tissue and carcinogenesis. It is known today that ROMs activate crucial

processes involved in cell growth, and in processes that inhibit programmed cell death, one of the main mechanisms involved in cancer control," De Censi said.

Therefore, researchers are testing the effect of ROM scavengers, such as allopurinol, to measure their effects on chemoprevention. According to De Censi, previous research from a large case-control study conducted in Israel showed that patients under chronic allopurinol use for gout had a lower risk for colorectal cancer than a matched control group not using allopurinol.

In the current study, De Censi and colleagues conducted a Phase I/II double-blind, placebo-controlled trial of patients with colorectal adenomatous polyps. Between 2006 and 2010, 73 patients were enrolled and assigned placebo or either a 100-mg or 300-mg dose of allopurinol for four to six weeks prior to removal of polyps.

They collected normal and adenomatous tissue samples and measured changes in the biomarker Ki67 in the normal tissue and the adenomatous tissue to measure the effect of allopurinol. At an interim analysis, conducted in November of 2008, only three mild adverse gastrointestinal events had occurred, confirming the high safety profile of allopurinol.

Tissue analysis in the first 13 patients indicated that levels of Ki67 in normal tissue had doubled in patients taking placebo, but had only increased by 5 percent in patients taking either dose of allopurinol.

In adenoma tissue, levels of Ki67 increased by 70 percent in patients taking placebo compared with only 6 percent in patients taking 100 mg allopurinol and 12 percent in patients taking 300 mg allopurinol.

"Our findings need to be confirmed on a larger number of subjects. However, if the positive trend noted on Ki67 is confirmed, we will

conclude that allopurinol has some activity against colon carcinogenesis that may explain the favorable trend noted in the epidemiological studies. These results will provide the background for a large trial of adenoma recurrence reduction with allopurinol," De Censi said.

Provided by American Association for Cancer Research