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UCI study finds effective colon cancer prevention treatment

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Using a combination of a targeted cancer-fighting agent called DFMO and a low dose of an anti-inflammatory drug, UC Irvine researchers have reduced the risk of reoccurring colorectal polyps, an early sign of colon cancer, by as much as 95 percent with fewer toxic side effects.

The study marks a breakthrough in the effort to combat colon cancer, the third leading cause of cancer in men and fourth in women, according to Dr. Frank L. Meyskens Jr., the Daniel G. Aldrich Chair at UC Irvine and director of its Chao Family Comprehensive Cancer Center.

“There is a great hope that we will be able to prevent colon cancer effectively using this method,” said Meyskens, who led the clinical trial effort to test this drug combination. He will present his findings April 14 at the American Association for Cancer Research annual meeting in San Diego.

In earlier studies, Meyskens had established a safe and well-tolerated dose of DFMO (difluoromethylornithine) that was 1/50 of what would typically be used to treat advanced cancers. By combining this reduced dose of DFMO with a non-steroidal, anti-inflammatory drug called sulindac, researchers believed they could improve treatment and decrease the reoccurrence of potentially cancerous colon polyps with reduced toxic side effects.

DFMO is the basis of the drug eflornithine, which was initially developed as a cancer medication and is no longer manufactured

commercially for that purpose. Sulindac is sold commercially as Clinoril and is used to treat arthritis and other inflammatory conditions.

The researchers enrolled 375 patients who had a history of at least one colorectal polyp, or adenoma, within the previous five years. Patients were randomly assigned to either a combination of 500 mg of daily DFMO and 150 mg of sulindac or placebos. Patients were followed for three years, and adenoma recurrence was measured by colonoscopy. Among the results:

-- Overall risk for recurrent adenoma: 41.1 percent in placebo group to 12.3 percent in treated patients, a 79 percent reduction

-- Risk for recurrent advanced adenomas: 8.5 percent in placebo group to 0.7 in treated patients, a 92 percent reduction

-- Risk for adenomas larger than one centimeter: 7 percent in the placebo group to 0.7 percent in the treatment group, a 90 percent reduction.

-- Rate of repeating adenoma among patients who had previously had more than one adenoma: 13.2 percent in the placebo group to with 0.7 percent in the treatment group, a 95 percent reduction.

The rate of reduction was so pronounced that the trial's independent data and safety monitoring board stopped the trial early.

An analysis of side effects and toxicity found no difference between the treatment and placebo groups. There also was no difference in side effects requiring an overnight hospitalization, gastrointestinal side effects or cardiovascular side effects between the two groups.

"What we have shown here is that there is value in testing these agents at

lower doses and in combination to determine if we can achieve the same effect without the damaging side effects," Meyskens said.

Source: University of California - Irvine