New treatment reduces precancerous polyps in hereditary cancer patients

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Inheriting a mutation in the APC gene leads to a nearly 100% lifetime risk of colorectal cancer. While colon cancer can be kept at bay by removing the large intestine, these patients also have up to a 15% risk of getting cancer in the small intestine, which is the leading cause of cancer death in this patient group. A new study published in the *Journal of the American Medical Association (JAMA)*, has identified the first prevention treatment for these patients, a two-drug combination that significantly reduces the number and size of precancerous polyps in the small intestine.

Jewel Samadder, MD, is the lead researcher on the study from Huntsman Cancer Institute (HCI) at the University of Utah. He says that medical and surgical management of these patients is difficult since it is hard to remove precancerous polyps in the small intestine and surgical removal of this region of the small, as well as the large intestine, means that patients have a hard time absorbing nutrients. "We have been left with very few, really no options to offer treatment."

Familial adenomatous polyposis (FAP) is an inherited disorder that occurs in 1 out of 10,000 people. It is caused by a mutation in the APC (adenomatous polyposis coli) gene that is inherited from one parent. Patients with FAP form hundreds to thousands of polyps in their large and small intestine. Many patients have their large intestine removed to prevent colon cancer, but for some patients with a large number of small intestine polyps, it is difficult to prevent cancer from occurring.

Research studies using cultured colon cancer cells and in a mouse model for FAP, suggested that blocking two different biochemical pathways at the same time may inhibit cancer growth. Specifically, in the mouse FAP model, giving a drug that blocked an inflammation pathway driven by cyclooxygenase-2 (COX-2) and a drug that blocked the epidermal growth factor receptor (EGFR), reduced the development of small intestine cancer in the animals by 87%.

Deborah Neklason, PhD, a researcher on the study, says the current clinical trial used the information obtained in basic science to test a drug combination of sulindac (inhibitor of COX-2) and erlotinib (inhibitor of EGFR). "This trial is an effort to go at two pathways that intersect and see if we could drive down the development of polyps and cancer in the small intestine," says Neklason.

Ninety-two FAP patients were identified from the Huntsman Cancer Institute Hereditary Gastrointestinal Cancer Registry, one of the largest registries in the world, and were entered into a trial where half received drug and half placebo. The trial was blinded so neither the patients nor researchers knew who was getting the drug. Both groups of patients received an endoscopy before the trial began and again after six months in order to visualize and characterize the size and number of polyps before and after treatment.

At the time of the six-month endoscopy, the drug treatment group had significantly fewer (p