Infliximab Cuts Ulcerative Colitis Colectomy Rate

BY MITCHEL L. ZOLER
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PHILADELPHIA — Patients with moderate to severe ulcerative colitis treated with infliximab had their colectomy rate cut by more than a third during the first year of treatment, compared with control patients, according to a review of more than 600 patients enrolled in two pivotal studies.

The results will likely be important for physicians who must decide whether a patient with advanced ulcerative colitis (UC) should start treatment with a biologic drug that blocks tumor necrosis factor–α (TNF-α).

"These are unique data that show we can alter the natural history of the disease," Dr. Brian G. Feagan said at the annual meeting of the American College of Gastroenterology. It's increasingly understood that colectomy is not a complete solution for advanced UC because of the risks of pouchitis, reduced fecundity, and other complications, added Dr. Feagan, professor of medicine in the gastroenterology service, University of Western Ontario, London.

UC patients "in remission with their colon have a better quality of life" than patients who undergo colectomy, commented Dr. Stephen B. Hanauer, professor of medicine and chief of gastroenterology at the University of Chicago. "Chronically sick patients benefit from colectomy, but the goal of treatment is to get patients in remission and off steroids. Biologic treatments can do this," he said in an interview.

The new analysis used data collected in the Active Ulcerative Colitis Trials 1 and 2 (ACT 1 and ACT 2), which together compared two dosages of infliximab (either 5 mg/kg or 10 mg/kg) with placebo in two different protocols that treated patients for as long as 54 weeks. The primary finding was that patients treated with either dosage were more likely than placebo patients to have a clinical response after 8, 30, and 54 weeks of treatment (N. Engl. J. Med. 2005;353:2462-76). This led to Food and Drug Administration approval of infliximab (Remicade) for treating moderately to severely active UC.

The ACT 1 and 2 studies were sponsored by Centocor Inc., which markets infliximab in the United States, and by Schering-Plough, which markets the drug in all other countries. Dr. Feagan and Dr. Hanauer receive research support from, and are consultants to and speakers for Centocor.

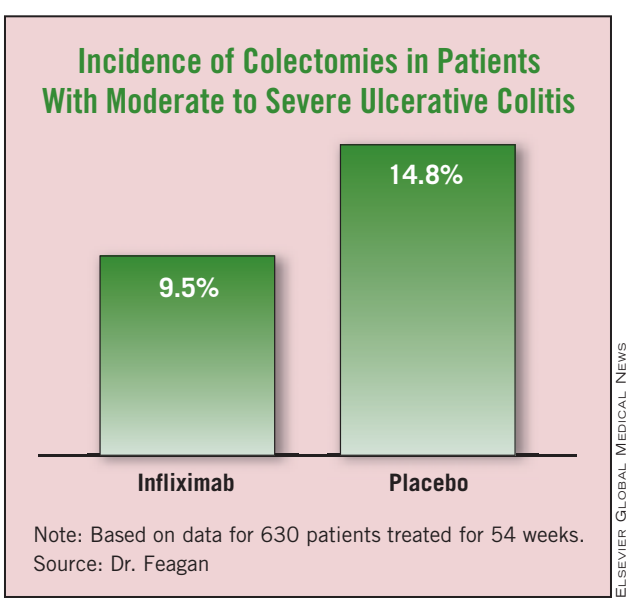
Data on the incidence of colectomy during the first year of treatment with infliximab were not collected for all patients in the two studies. This information was available from trial records for about half of the patients. Additional information was collected through retrospective contact with patients. About 14% of patients in the study were excluded because no data on their colectomy status were available, leaving 630 patients in the new analysis.

The incidence of colectomies was 9.5% among all patients treated with infliximab during 54 weeks of treatment, compared with a 14.8% rate in the placebo group, a 5.3% absolute cut in the rate of surgery that was statistically significant and a 43% relative reduction, Dr. Feagan said.

Further analysis showed that several patients who received only 30 weeks of placebo treatment by the study protocol were crossed to infliximab during an extension phase. The incidence of either colectomy or the start of infliximab treatment was cut in half in the infliximab-treated patients, compared with the control group.

Infliximab treatment also was linked to significant reductions in hospitalizations for UC, and in surgical and endoscopic procedures of all kinds.

The adverse event profile for infliximab was similar to what was reported in 2005 for the ACT 1 and 2 studies, with no additional cases of tuberculosis, demyelinating disease, or hematologic events, Dr. Feagan said. ■



Number of Adenomas, Rather Than Size, Are Predictors of Colonic Recurrence Risk

BY MITCHEL L. ZOLER
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PHILADELPHIA — A finding of three or more adenomas on colonoscopy was the strongest predictor of identifying high-risk individuals on follow-up colonoscopy in a review of 800 patients with colonic adenomas identified during their baseline examination. Those are individuals that harbor more than two large or histologically advanced neoplasms.

"When doing colonoscopy, we must be diligent about identifying synchronous neoplasia, regardless of size, in order to identify high-risk people" who need more frequent colonoscopy exams, Dr. Carol A. Burke said at the annual meeting of the American College of Gastroenterology.

An adenoma count of three or more was a stronger predictor of having numerous or advanced adenomas on the next colonoscopy, which was more important than adenomas 1 cm or greater in size of advanced pathology, said Dr. Burke, director of the Center for Colon Polyps and Cancer Prevention at the Cleveland Clinic.

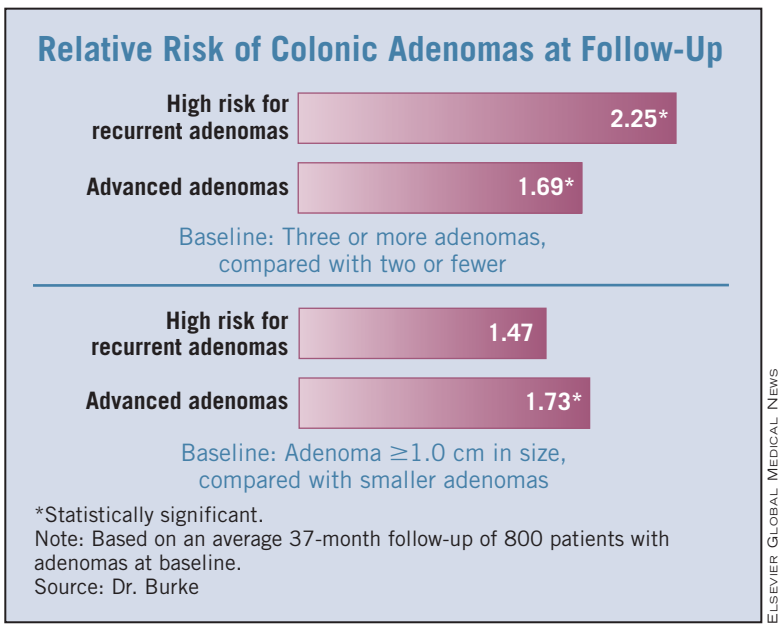
For colonic adenomas, "what's important is number, number, number," she said in an interview.

Her study compiled data from the placebo groups of three postpolypectomy chemoprevention trials that were conducted during the mid-1980s to late 1990s. For inclusion in the new analysis, patients could not have colorectal cancer at baseline, and they had to have a follow-up colonoscopy about 3 years after they entered one of the included trials.

A total of 800 patients met these criteria, and their average age was 60 years. Follow-up colonoscopy was done an average of 37 months after the baseline examination.

Demographic and clinical findings during the baseline colonoscopy were assessed as predictors of identifying a high-risk individual on follow-up colonoscopy after 3 years. Those individuals have either advanced adenomas or more than two adenomas on the second colonoscopy. In both the univariate and multivariate analyses, more than two adenomas was the only predictor of both advanced neoplasms (defined as those that were 1 cm or greater in size and had significant villous pathology) or more than two adenomas on follow-up.

The take-home message from these findings is that physicians should not discount the importance of detecting numerous adenomas, regardless of size on colonoscopy, Dr. Burke said. ■



Mesalamine, Folic Acid Cut Cancer Risk in IBD

PHILADELPHIA — Treatment with either folic acid or mesalamine was linked to about a 90% reduction in the incidence of colorectal cancer in a case-control study including 48 patients with inflammatory bowel disease.

Both agents "appear to be very promising cancer chemopreventive agents," but the findings need to be confirmed in additional inflammatory bowel disease (IBD) patients, Dr. Jeffrey Tang said at the annual meeting of the American College of Gastroenterology.

The analysis showed that patients who took a cumulative dose of at least 4,500 g of mesalamine had a statistically significant, 91% drop in their incidence of colorectal cancer (CRC), said Dr. Tang, a gastroenterologist at Henry Ford Hospital in Detroit. The usual mesalamine dose used by IBD patients at Henry Ford was 1.6 g/day.

Patients who took at least 1 mg of folic acid daily also had about a 90% cut in their CRC incidence during follow-up, compared with the controls. Two additional analyses showed that the effects of mesalamine and folic acid on CRC prevention were completely independent of each other.

Dr. Tang and his associates reviewed the records of 1,784 patients with IBD who were seen at Henry Ford Hospital during 1970-2005. Thirty of the patients developed CRC during an average follow-up of 8 years; 25 had ulcerative colitis and 5 had Crohn's disease.

The researchers then attempted to match each of the incident cases with up to two control patients with IBD who did not develop CRC during an average follow-up of 12 years. A total of 30 control patients were identified to match with 18 of the incident cases. No matches were found for the remaining 12 IBD patients who developed cancer during follow-up, and they were dropped from the analysis. The cases and controls were very similar on several parameters, including gender, race, and family history of IBD.

—Mitchel L. Zoler