Ulcerative Colitis Patients Benefit From Infliximab

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.

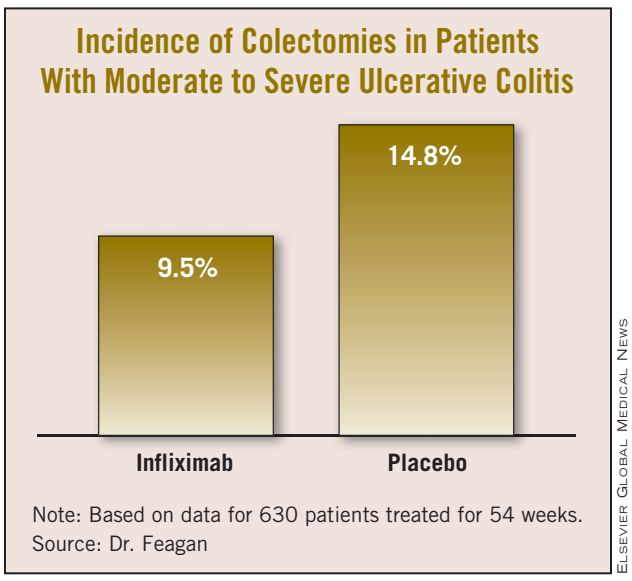
The results will likely be important for physicians who must decide whether a patient with advanced ulcerative colitis (UC) should start treatment with a biologic drug that blocks tumor necrosis factor–α (TNF-α).

"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, he said in an interview.

"These data add more fuel to the debate about medical therapy versus surgery" for patients with advanced UC, added Dr. Feagan, professor of medicine in the gastroenterology service, University of Western Ontario, London. "Which is more desirable: chronic immunosuppression [with a biologic drug] or colectomy? You can't say that one size fits all patients."

"It seems like infliximab may alter the natural course of UC by reducing the need for colectomy," commented Dr. Miguel D. Regueiro, codirector of the inflammatory bowel disease center at the University of Pittsburgh. Physicians and patients will need to decide whether the risks and complications of colectomy are high or low compared with biologic therapy, and whether quality of life is better with colectomy or biologic therapy, he said.

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 cholectomy, but the goal of treatment is to get patients in remission and off steroids. Biologic treatments can do this," he said in an interview.



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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. Dr. Regueiro receives research support from and is a consultant to 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 colectomy was 9.5% in 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. ■

Complications Accumulate After Colectomy

Colectomy may cure ulcerative colitis, but not without a price to patients.

Follow-up of 47 patients with ulcerative colitis (UC) who underwent colectomy at the Mayo Clinic during 1970-2001 revealed a complication rate of about 800 per 1,000 patient-years of follow-up in the first 2 years after surgery, Dr. Salma Akram reported at the annual meeting of the American College of Gastroenterology.

The complication rate slowed substantially after the first 2 years. The cumulative rate of a first complication was 43% in the first year after surgery, 68% after 5 years, and 74% after 10 years, said Dr. Akram, a former gastroenterology fellow at the Mayo Clinic in Rochester, Minn. In a cohort study limited to patients who were residents of Olmsted County, Minn., the most common complications were wound infections, small-bowel obstructions, and pouchitis. The type of surgery, usually total proctocolectomy either with ileostomy or with a pouch, was not significantly linked to the complication rate.

In a separate talk at the meeting, Dr. Regueiro said that other complications of colectomy include a substantial reduction in fecundity in young women, impotence in men, other pouch complications, and mortality in a small number of patients (less than 0.5%).

Two drugs have a record for treating advanced UC—infliximab and cyclosporine. The long-term impact of infliximab on UC has not yet been reported, but with cyclosporine about 90% of patients had recurrences within 5 years, including 60% who eventually needed surgery, Dr. Regueiro said.

Patient Satisfaction High Following Ileoanal Pouch Surgery

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

NEW ORLEANS —Long-term functional outcomes may decline after ileoanal pouch surgery, but most patients report higher a quality of life than they had before their surgery, Dr. Feza H. Remzi said at the annual clinical congress of the American College of Surgeons.

Dr. Remzi of the Cleveland Clinic Foundation reported the results of a long-term follow-up study of 3,080 patients who underwent ileoanal pouch formation at the clinic from 1983 to 2006.

The patients' mean age at surgery was 38 years. Most (87%) had a final diagnosis of ulcerative or indeterminate colitis. A total of 43% of patients underwent surgery because of failed medical therapy or steroid dependence. Some of the other indications were prior colectomy (33%); dysplasia, cancer, or cancer prevention (11%); and familial polyposis (4%). The most commonly performed surgical technique was a stapled anastomosis (78%). A J-pouch design was used in 82% of patients, and 17% had their pouches created with no need for a diverting ileostomy.

The 30-day complication rate was low. Wound infections occurred in 5% of patients, small bowel obstruction in 4%, sepsis in 4%, postoperative bleeding in 3%, anastomotic separation in 2.5%, and fistula in 1%. Less than 1% of patients had pouch failure in the first 30 days.

At 5-15 years after surgery, however, all complications (sepsis, fistula, anastomotic stricture, obstruction, pouch failure, and pouchitis) had a tendency to increase. Significant increases were seen in small bowel obstruction (from 16% at 5 years to 23% at 15 years) and pouchitis (from 32% to 52% over that same period).

Incontinence increased significantly over time. Although 75% of patients reported complete continence at 3 months post operatively, only 32% reported it 15 years later. But there were some significant long-term improvements. Before surgery, only 60% of patients reported rare incontinence or none at all. By 3 months after surgery, the percentage of that combined group of patients had risen to 80%, and it did not vary significantly during the next 15 years of follow-up.

There was no significant change in the number of daytime or nighttime bowel movements from baseline to 15 years. Urgency decreased significantly over the same period. However, pad usage and seepage increased.

Nonetheless, patients generally reported high quality of life scores as early as 3 months after the procedure, and these scores stayed high throughout the follow-up period, Dr. Remzi said. All patients reported significant decreases in dietary, work, social, and sexual restrictions at each time period.

In discussing the paper, Dr. Robin McLeod stressed that quality of life should be a primary end point in any evaluation of long-term outcomes after this procedure. "Although the functional outcomes are not perfect, the quality of life for these patients is very good, and they are happy with the procedure. This is one of the disconnects that can happen when we focus only on the functional outcome and don't look at the patient globally," said Dr. McLeod of Mount Sinai Hospital, Toronto.

According to Dr. Remzi, 97% of patients said they would undergo the procedure again, and would recommend it to others. "This is a very important indication of quality of life—that they would do it all over again," he said. ■