Infliximab Effective for Active Ulcerative Colitis

In two phase III trials, the drug reduced symptoms, induced remission, and led to mucosal healing.

BY KATHLEEN LOUDEN
Contributing Writer

CHICAGO — Active ulcerative colitis responds to the drug infliximab, according to results of two multicenter phase III trials reported at the annual Digestive Disease Week.

Active Colitis Trial (ACT) 1 and ACT 2 each enrolled 364 patients with moderate or severe ulcerative colitis, refractory to at least one standard therapy.

Investigators randomized patients to receive infliximab at a 5 mg/kg dosage, a 10 mg/kg dosage, or placebo at baseline and at weeks 2 and 6, and then every 8 weeks through week 46.

After 8 weeks of infliximab therapy at either dosage, more than 60% of patients in each trial demonstrated improvement in their symptoms vs. approximately 29% and 37% of placebo-treated patients in ACT 1 and 2, respectively, the authors reported. At 30 weeks, the clinical response was still significantly better in the infliximab groups.

Infliximab also effectively induced remission and led to mucosal healing in patients with active ulcerative colitis, both studies showed.

"This is very encouraging news for a patient population that has few treatment options," said William Sandborn, M.D., principal investigator of ACT 2 and head of the Mayo Clinic College of Medicine's irritable bowel disease interest group and clinical research unit.

Both ACT 1 and 2 trials had similar results and patient populations, according to Dr. Sandborn, whose institution was one of 55 study centers. He described subjects as outpatients with relatively stable disease.

Several differences between the studies existed, however. At enrollment, ACT 1 patients had not responded to treatment with corticosteroids and/or immunosuppressive therapy, whereas patients in ACT 2 had experienced treatment failure with 5-aminosalicylates, steroids, and/or immunosuppressives. The duration of ACT 1 also was longer (54 vs. 30 weeks).

Clinical response was defined as a decrease in the Mayo score of at least 30% and 3 or more points, plus either a reduction of 1 or more points in the rectal bleeding score or a score of 0 or 1 at week 8.

In addition to clinical response, both trials studied clinical remission—a Mayo score of 2 or less, with no individual subscores greater than 1—and mucosal healing, characterized as an endoscopy subscore of 0 or 1.

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DR. SANDBORN

Remission rates for the drug-treated patients were as high as 39% in ACT 1 (5 mg/kg) at week 8, compared with 15% for placebo. In ACT 1, the difference in the patients' 8-week remission rates between the 10 mg/kg infliximab dosage (32%) and placebo was highly statistically significant, said that trial's lead investigator, Paul Rutgeerts, M.D., from the University Hospital, Leuven, Belgium. Dr. Rutgeerts is a grant recipient of Centocor, the manufacturer of infliximab (Remicade).

Significant differences in remission rates between infliximab and placebo also were evident in ACT 2 and continued at 30 weeks in both trials.

Mucosal healing occurred at week 30 in a higher percentage of patients receiving 10 mg/kg of infliximab than in those with the smaller dosage (50% vs. 49% in ACT 1; 57% vs. 46% in ACT 2). Healing rates for both dosages were significantly higher than for placebo (25% in ACT 1; 30% in ACT 2).

In each study, the proportion of patients who were in remission and able to stop use of corticosteroids after 30 weeks of infliximab therapy was significantly greater for both dosages, compared with placebo.

Adverse effects seen in ACT 2 patients receiving infliximab included five cases of pneumonia and one case each of tuberculosis, optic neuritis, multifocal neuropathy, and lupus-like syndrome, Dr. Sandborn reported.

Dr. Sandborn is also a grant recipient of Centocor. ■

Noninvasive Indices May Suffice To Evaluate Ulcerative Colitis

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Endoscopy is an invasive procedure that patients don't like, and it may not be necessary for the evaluation of ulcerative colitis, Peter Higgins, M.D., said at the Clinical Research 2005 meeting.

In a study of 66 consecutive adult ulcerative colitis patients, results from two noninvasive indices overlapped significantly with results from invasive indices, said Dr. Higgins of the University of Michigan, Ann Arbor, and his colleagues.

Regular use of noninvasive indices to assess ulcerative colitis could lower costs and encourage more patients to participate in clinical trials, he noted.

The investigators compared invasive and noninvasive indices in terms of how well each measured disease remission and other clinically important outcomes. The invasive indices used were the St. Mark's Index and the Ulcerative Colitis Disease Activity Index (UCDAI), which involved endoscopy, and the noninvasive indices were the Simple Clinical Colitis Activity Index (SCCAI) and the Seo index, which involved short symptom surveys and blood tests. In addition, the doctors simply asked patients whether their disease was in remission.

Other indices are available in addition to those used in this study, Dr. Higgins said. "The problem is that none of them are validated, and none of them work that well."

The investigators measured the correlations between the various indices to determine whether the noninvasive tests could provide similar information to that provided by the invasive tests. The two noninvasive indices, SCCAI and Seo, correlated well with the invasive St. Mark's index, with correlations of 0.86 for the SCCAI and 0.70 for Seo.

When the two invasive indices were compared with each other, the UCDAI endoscopy item predicted only 0.04% of the variance in the St. Mark's index after adjustment for the three noninvasive items on the UCDAI index.

Overall, endoscopy contributed little to the assessment—significantly less than the 10% that Dr. Higgins expected. "We may not need endoscopy" to evaluate ulcerative colitis patients, he said.

One explanation for endoscopy's minor role might be that other items on the same scale have measured the same predictive factors, such as patient-reported stool frequency and the frequency and amount of blood in the stool, which would make endoscopy redundant, he explained.

Dr. Higgins concluded that noninvasive indices could effectively predict remission. "We're not losing much by leaving out endoscopy," he said.

The clinical practice of treating patients based on their reported symptoms is appropriate, and clinicians are correct to avoid rushing to scope. "If the patient tells you they have 10 bloody stools, they are having a flare," he said at the meeting, sponsored by the American Federation for Medical Research.

"The best arbiter of remission is the patient," he added, inasmuch as the patient will choose whether to seek additional health care. ■

Women With Ileal Pouches Report Negative Effects on Sexual Function

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Women who underwent an ileal pouch/anal anastomosis procedure for ulcerative colitis reported impaired sexual function, compared with historic, normal controls, Laura H. Goetz, M.D., said at the annual meeting of the American Society of Colon and Rectal Surgeons.

The etiology of worsened sexual function, found in a survey of 92 patients, is unclear. It might be caused by nerve damage during proctectomy, inadequate pouch function, or simply aging, said Dr. Goetz, a colon and rectal surgeon at the University of California, San Francisco.

Worsened sexual function, found in a survey of 92 patients, might be caused by nerve damage during proctectomy, inadequate pouch function, or simply aging.

A questionnaire was used to assess sexual function in women who had undergone the ileal pouch/anal anastomosis procedure. The questionnaire included the modified Female Sexual Functioning Index (FSFI), the Fecal Incontinence Severity Index, and additional questions about pouch function. It was sent to 167 women who had surgery for ulcerative colitis during 1990-2004 at UCSF. Of those, 92 women returned completed surveys. Their mean age was 39.5 years, with a range of 19-61 years. The questions were answered a mean of 6 years after surgery, with a range of 1-14 years.

The average score on the modified FSFI was 23.9. The highest score possible on this index is 36.0, which would indicate no impairment. The previously published average score of healthy women was 30.5.

The average score of women in the current study was higher than that reported in prior studies of women with sexual-arousal disorders, whose average score was 19.2. In the surveyed group, 26% of the women had scores greater than 30, and another 26% had scores less than 20.

The FSFI score also varied by age, with women younger than age 50 having an average score of 25, and women older than age 50 having an average score of 18.

When scores were compared before and after surgery, 24% of the women had their scores improve after surgery and 43% had their scores worsen; the rest had no change.

The FSFI scores of the surveyed women did not correlate at all with their Fecal Incontinence Severity Index scores.

There was also no correlation with fecal frequency, urgency, or fear of leakage, although women who experienced actual leakage during sex did have lower sexual function scores. ■