

Crohn's Disease Treatment With Infliximab, Azathioprine, or Combination Therapy

An April issue of *The New England Journal of Medicine* reported results of a randomized, double-blind, multicenter trial conducted by the international SONIC Study Group assessing the efficacy of infliximab monotherapy, azathioprine monotherapy, and infliximab plus azathioprine combination therapy. The patient population consisted of 508 adult patients with moderate-to-severe Crohn's disease who were naive to immunosuppressive or biologic therapy. Patients underwent random assignment to: intravenous infusion of 5 mg/kg of infliximab at Weeks 0, 2, and 6 and then every 8 weeks plus daily oral placebo capsules; 2.5 mg/kg of oral azathioprine daily plus a placebo infusion on the standard schedule; or combination therapy with both drugs. Patients still in the trial at Week 30 were offered the option of continuing in a blinded extension trial for 20 additional weeks.

In the combination therapy arm (n=169), 96 (56.8%) patients experienced corticosteroid-free clinical remission at Week 26 (which had been established as the primary endpoint) compared to 75 of 169 patients (44.4%) in the infliximab monotherapy arm ($P=.02$) and 51 of 170 patients (30.0%) in the azathioprine monotherapy arm ($P<.001$ when compared to combination therapy and $P=.006$ when compared to infliximab monotherapy). These results were durable through Week 50. At Week 26, 47 of 107 patients (43.9%) in the combination therapy arm experienced mucosal healing compared to 28 of 93 patients (30.1%) in the infliximab arm ($P=.06$) and 18 of 109 patients (16.5%) in the azathioprine monotherapy arm ($P<.001$ when compared to combination therapy and $P=.02$ when compared to infliximab monotherapy). Serious infections were found in 3.9% of the combination therapy arm, 4.9% of the infliximab monotherapy arm, and 5.6% of the azathioprine monotherapy group.

Rapid Response to Cognitive Behavior Therapy for Irritable Bowel Syndrome

Researchers at the University at Buffalo, State University of New York conducted a study of irritable bowel syndrome patients to determine whether rapid responders to cognitive behavior therapy maintained their treatment gains compared to nonrapid responders. The study, which was published in the May issue of *Clinical Gastroenterol-*

ogy and Hepatology, was comprised of 71 patients (age, 18–70 years old) with irritable bowel syndrome based upon Rome II criteria that was at least moderately severe. Patients underwent random assignment to: a wait list control; 10 weekly 1-hour sessions of cognitive behavior therapy; or four 1-hour cognitive behavior therapy sessions over 10 weeks. Rapid responders were defined as those who experienced adequate relief of pain and bowel symptoms as well as a reduction in irritable bowel syndrome severity scores of at least 50 by Week 4.

The researchers found that rapid responders comprised 30% of the patients undergoing cognitive behavior therapy, and 90–95% of these patients maintained their gains at the immediate and 3-month follow-ups. At baseline, rapid responders experienced more severe irritable bowel syndrome symptoms; however, they achieved more substantial and sustained symptom reduction compared to nonrapid responders. Each of the cognitive behavior therapy arms experienced comparable rates of rapid responders.

Once-Only Flexible Sigmoidoscopy Screening for Prevention of Colorectal Cancer

Researchers at the Imperial College London in the United Kingdom conducted a multicenter, randomized controlled trial to evaluate the hypothesis that only one flexible sigmoidoscopy screening between the ages of 55 and 64 could result in a substantial reduction in the incidence and mortality of colorectal cancer. The results of this study, which were recently released online ahead of print publication in *Lancet*, involved 170,432 eligible men and women in 14 UK centers who had noted on an earlier questionnaire that they would accept an invitation for screening. The patients were randomly assigned to either the intervention arm (and offered flexible sigmoidoscopy screening) or the control arm (and were not contacted). Recruitment and screening were started in November of 1994 and completed in March of 1999.

A total of 113,195 people were assigned to the control arm and 57,237 to the intervention arm, and 112,939 and 57,099 people, respectively, comprised the final analyses. A total of 40,674 (71%) people underwent flexible sigmoidoscopy. Over a screening and median follow-up period of 11.2 years (IQR, 10.7–11.9), colorectal cancer was detected in 2,524 people (1,818 in the control arm vs 706 in the intervention arm) and 20,543 people

died (13,768 in the control arm vs 6,775 in the intervention arm, though only 727 deaths were certified from colorectal cancer [538 vs 189, respectively]). According to intention-to-treat analyses (which included people assigned to screening but who did not attend), the incidence of colorectal cancer in the intervention arm decreased by 23% (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.70–0.84) and mortality decreased by 31% (HR, 0.69; 95% CI, 0.59–0.82). According to per-protocol analyses (adjusted for self-selection bias in the intervention arm), the incidence of colorectal cancer in people attending screening decreased by 33% (HR, 0.67; 95% CI, 0.60–0.76) and mortality decreased by 43% (HR, 0.57; 95% CI, 0.45–0.72). Distal colorectal cancer incidence decreased by 50% (HR, 0.50; 95% CI, 0.42–0.59; the secondary outcome). The numbers needed to be screened to prevent 1 colorectal cancer diagnosis or death, by the end of the study period, were 191 (95% CI, 145–277) and 489 (95% CI, 343–852), respectively. The researchers also pointed out that 59% (126) of the 215 colorectal cancer cases that developed were detected at screening and very few cases were detected postscreening, suggesting that screening has a lasting protective effect.

Open Necrosectomy Versus Step-up Treatment for Necrotizing Pancreatitis

According to an April issue of *The New England Journal of Medicine*, researchers at the University Medical Center in Utrecht, The Netherlands conducted a multicenter study to evaluate treatment options for patients with necrotizing pancreatitis. In this study, 88 patients with necrotizing pancreatitis and suspected or confirmed infected necrotic tissue were randomized to either primary open necrosectomy (considered the standard treatment of these patients) or step-up therapy (ie, percutaneous drainage followed by minimally invasive retroperitoneal necrosectomy, if needed). A composite of major complications (including new-onset multiple-organ failure or multiple

systemic complications, perforation of a visceral organ or enterocutaneous fistula, or bleeding) or death comprised the primary endpoint of the study.

The researchers reported that the primary endpoint occurred in 31 of the 45 patients (69%) in the open necrosectomy arm and in 17 of the 43 patients (40%) in the step-up treatment arm (risk ratio with step-up therapy, 0.57; 95% CI, 0.38–0.87; $P=.006$). Among the patients receiving step-up therapy, 35% underwent only percutaneous drainage. Patients in the step-up arm experienced new-onset multiple-organ failure less frequently than those in the open necrosectomy arm (12% vs 40%; $P=.002$). There was no significant difference in the rate of death between the 2 arms (19% vs 16%; $P=.70$).

In Brief

In a prospective study, vitamin E was superior to placebo for the treatment of nonalcoholic steatohepatitis in adults without diabetes. No benefit was noted for pioglitazone over placebo for the primary outcome; however, significant benefits of pioglitazone were observed for some of the secondary outcomes. *N Engl J Med.* 2010 Apr 28. [Epub ahead of print].

According to a systematic review of data from 32 studies, *Helicobacter pylori* eradication is effective in treating approximately 75% of patients with early-stage gastric lymphoma. Long-term follow-up evaluation of these patients is needed to detect early lymphoma relapse or progression. *Clin Gastroenterol Hepatol.* 2010;8:105-110.

Researchers of a retrospective, single-center analysis of postendoscopic submucosal dissection bleeding concluded that a second-look endoscopy after gastric endoscopic submucosal dissection may contribute little to the prevention of delayed bleeding. *Gastrointest Endosc.* 2010;71:241-248.