Certolizumab Shown Safe And Effective for Crohn's

BY MITCHEL L. ZOLER
Philadelphia Bureau

COPENHAGEN — A new, anti–tumor necrosis factor antibody was safe and effective for treating Crohn's disease for 26 weeks in a study with more than 400 patients.

Certolizumab pegol was better than placebo for maintaining responses in patients with Crohn's disease following induction, Stefan Schreiber, M.D., said at the 13th United European Gastroenterology Week.

A second Crohn's disease study of certolizumab (Cimzia), a pegylated form of a humanized antibody fragment, is in progress, and patients from both studies will continue to receive the drug for 2 years to gather further safety information. UCB, the Belgium company developing Cimzia, plans to submit all the data early next year to the Food and Drug Administration to apply for a new-drug approval.

Certolizumab is the third anti–tumor necrosis factor (TNF) antibody to be tested on patients with Crohn's disease. Infliximab (Remicade) is already approved for this indication. Adalimumab (Humira) is approved for treating rheumatoid arthritis and psoriatic arthritis, and is being studied in patients with Crohn's disease.

Certolizumab and adalimumab are both administered by subcutaneous injection, making them more convenient treatments than infliximab, which must be administered by intravenous infusion. Studies that are underway are also assessing certolizumab in patients with rheumatoid arthritis.

The study reported by Dr. Schreiber began with 668 patients who had a Crohn's disease activity index (CDAI) score at baseline of 220-450 points, indicating active disease.

All patients received three 400-mg doses of certolizumab, given at 2-week intervals. Following the induction phase, 428 patients (64%) had a clinical response, defined as a drop in their CDAI score of at least 100 points.

The fraction of patients who responded to certolizumab was similar in size to the fraction who responded to infliximab and adalimumab in prior studies, Dr. Schreiber said.

The responders were then randomized to a maintenance regimen of 400 mg certolizumab injected every 4 weeks or placebo, for an additional 22 weeks.

After a total of 26 weeks of treatment, 63% of patients who continued on certolizumab remained responders, with at least a 100-point improvement in their CDAI score compared with baseline, and 36% of patients in the placebo group responded, for a statistically significant difference, said Dr. Schreiber, professor of medicine and gastroenterology at Christian-Albrechts University in Kiel, Germany.

Similar levels of response were seen in patients who entered the study with high serum levels of C-reactive protein, in patients who were on immunosuppressive drugs at baseline, and in patients who had previously failed treatment with infliximab.

The percentage of patients who reached remission, defined as a CDAI score of 150 or less, was 48% of those maintained on certolizumab, compared with 29% of those who received placebo. In addition, 60% of patients maintained on certolizumab had an improved quality of life, compared with 43% in the placebo group.

The rate of serious adverse events was similar in the two study groups, and certolizumab was generally well tolerated, said Dr. Schreiber. One patient treated with the drug developed active tuberculosis.

An antibody reaction to the drug developed in 8% of patients. Although the effect of this reaction has not yet been assessed, the major potential impact is that the antibody might blunt the drug's benefit.

Although certolizumab has a similar mechanism of action as adalimumab and infliximab, the three drugs differ chemically and therefore probably differ in their biologic properties, Dr. Schreiber said. Compared with the other drugs, certolizumab has a lower protein content and is the only agent that is pegylated. ■

Infliximab First, Not Steroids, For Best Crohn's Treatment

BY MITCHEL L. ZOLER
Philadelphia Bureau

COPENHAGEN — Initial treatment with infliximab plus azathioprine in patients with moderate to severe Crohn's disease led to more remissions than did a standard approach that started with topical or systemic steroid treatment, in a study with 129 patients.

"Steroids are not necessary for treating Crohn's disease," said Geert D'Haens, M.D., at the 13th United European Gastroenterology Week.

"Our results strongly suggest that infliximab plus azathioprine, but without a steroid, is a superior regimen for moderate to severe, newly diagnosed Crohn's disease," said Dr. D'Haens, a gastroenterologist at Imelda Hospital in Bonheiden, Belgium. Further studies must compare various strategies to identify the best way to use biologic therapy to induce and maintain remission, he added.

The two management strategies were compared at 26 centers in Belgium and the Netherlands. The study enrolled patients with newly diagnosed Crohn's disease, a disease activity index of more than 220, and no prior treatment with a steroid or immunomodulator.

The study was sponsored by Centocor and Schering-Plough. Centocor markets infliximab (Remicade) in the United States, and Schering-Plough markets the drug in all other countries. Dr. D'Haens has served as a consultant and speaker for both companies.

The 65 patients in one group were randomized to treatment that started with three infusions of infliximab at weeks 0, 2, and 6, and daily treatment with 2-2.5 mg/kg azathioprine. Patients in this group who relapsed received another infusion of infliximab, and if they relapsed again they were treated with a steroid.

The remaining 64 patients were randomized to start treatment with either topical budesonide or oral prednisone, at a daily dose of 40 mg. Patients in this group who relapsed were again treated with a steroid plus azathioprine. If they relapsed a second time, they were treated with a three-dose course of infliximab.

Our results strongly suggest that infliximab plus azathioprine is a superior regimen for Crohn's.

DR. D'HAENS

The study's primary end point was the rate of remission at 6 and 12 months after starting treatment. Remission was defined as having a Crohn's disease activity index of less than 150, with no ongoing need for steroid treatment and no surgical resection.

After 6 months, the remission rate was 60% in the infliximab-first group and 41% among the patients who received steroid treatment first, a statistically significant difference, reported Dr. D'Haens.

After 12 months, the remission rate was 61% in the infliximab-first group and 50% among the steroid-first group, a difference that was not statistically significant.

Among patients in the infliximab-first group, 59% required no additional infliximab treatment beyond their initial three doses during the year of follow-up. In the steroid-first group, 62% of patients also required treatment with azathioprine.

The study also used a new measure of efficacy, the rate of overall treatment success. This measure tracked the number of patients who reached and maintained a remission after 14, 26, 39, and 52 weeks of treatment. This end point was reached by 29% of patients in the infliximab-first group and 5% of those treated with a steroid first, a statistically significant difference.

After the first 6 months of treatment, none of the patients in the infliximab-first group were on steroid treatment, while 31% in the steroid-first were on systemic prednisone.

After 12 months, no patients in the infliximab-first group were on steroid treatment, compared with 17% in the steroid-first group. Nine patients in the infliximab-first group had a serious adverse event that led to withdrawal from treatment, compared with 10 patients in the steroid-first group.

Curbing Inflammation May Reduce GI Cancer Risk in Crohn's

BY BOB BABINSKI
Contributing Writer

MONTREAL — The use of the immunosuppressive agent azathioprine and surgery reduced the risk of cancer in patients with Crohn's disease, according to an 11-year retrospective analysis.

"This study suggests that controlling the inflammation, or the disease activity, can reduce or eliminate any risk of GI-related cancer," Elizabeth Strevel, M.D., of the University of Toronto, said in an interview.

The investigation, which Dr. Strevel presented as a poster at the World Congress on Gastroenterology, used databases to review the cases of 1,351 Crohn's disease patients hospitalized at the city's teaching centers.

Sixty-five patients had one or more malignancies, with 37 of those originating in the gastrointestinal tract.

Patients who had a surgical intervention were at a decreased risk of malignancy of all types (odds ratio [OR] 0.4), as were patients who were given azathioprine (OR 0.4). A similar association was found for the use of steroids (OR 0.5).

"Our results showed that when we looked at all malignancies, indicators of increased inflammation, such as fistula, increased the risk of cancer," she said, noting an odds ratio of 1.7.

"That became more prevalent when we did a subgroup analysis, just in the GI cancer group. It indicated that what we found in the whole group was probably just an effect of the GI cancers," Dr. Strevel said.

"We also found that the effect of the immunosuppressive agent azathioprine also became more strongly protective in the subgroup, indicating that the effect is mostly on GI cancers."

Although cancer in Crohn's disease patients is quite rare, there is a need for more study, Dr. Strevel said."While malignancy isn't overly present in Crohn's disease, it is obviously a complication with a lot of morbidity and mortality."

"Given the numbers, it would be hard to do a randomized controlled trial. But a prospective cohort study following these people in a database, seeing what happens and assessing, will provide more accurate information," she added. ■