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Studies offer encouraging data on preventing Crohn's disease recurrence

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Biological agents may play an important role in maintaining remission in Crohn's disease, according to two new studies in *Clinical Gastroenterology and Hepatology*, the official journal of the American Gastroenterological Association (AGA) Institute.

"Post-surgical recurrence of Crohn's disease occurs very frequently. Unfortunately, none of the traditional drugs used to treat the naturally occurring disease has really shown a clear-cut benefit in this situation," said Dario R. Sorrentino, MD, of the University of Udine School of Medicine, Italy, and lead author of one of the studies. "Our study results indicate great potential for infliximab, a monoclonal antibody, which has shown remarkable efficacy in preventing this type of recurrence." Infliximab is known by the brand name Remicade®.

Doctors performed a prospective cohort study in 12 consecutive patients treated immediately after surgery with standard maintenance infliximab (5 mg/kg body weight every eight weeks) who did not have evidence of disease recurrence after 36 months. Treatment with infliximab was then discontinued. Patients with disease recurrence (i.e., with intestinal inflammation) were then given lower doses of infliximab in an attempt to re-establish the integrity of the intestinal mucosa, which helps ensure an adequate supply of nutrients.

The study authors showed that infliximab administration immediately after surgery effectively prevents recurrence of the disease (no intestinal inflammation and no symptoms) at three years. However, upon

suspension of the medication, intestinal inflammation appears after four months in the large majority of patients (83 percent), thus indicating the need for long-term uninterrupted maintenance therapy. Nevertheless, a 40 percent reduction from the standard dose of 5 mg/kg (i.e., a dose of 3 mg/kg) was sufficient to re-establish the integrity of the intestinal mucosa and avoid disease recurrence in all patients at one year.

"Additional studies may be needed to confirm our findings. However, lowering the dose of infliximab may be potentially safer and is more cost effective than standard dose strategies for prevention of post-operative recurrence of Crohn's disease. This should be considered in the long-term management of patients undergoing surgery for this indication," added Dr. Sorrentino.

In a second study published in Clinical Gastroenterology *and Hepatology*, doctors found that certolizumab pegol — another type of biologic therapy — effectively maintains remission of Crohn's disease for up to 18 months. In addition, continuous therapy is more effective than interrupted therapy. Certolizumab pegol is known by the brand name Cimzia®.

Subcutaneous certolizumab pegol administered every four weeks is an effective and well-tolerated, long-term maintenance therapy for patients with moderate to severe Crohn's disease. Continuous maintenance therapy with certolizumab pegol is more likely to produce response and remission than interrupted therapy, without negatively impacting patient safety.

Doctors assessed the long-term effectiveness, safety and immunogenicity (ability to create an immune response) of five continuous versus interrupted maintenance therapy with subcutaneous certolizumab pegol in patients with Crohn's disease. Patients who responded to induction therapy at week six of the PRECiSE 2 trial (one of two large, pivotal,

randomized, placebo-controlled, phase III studies) were randomly assigned to groups given certolizumab pegol (continuous) or placebo (drug-interruption). Patients who completed PRECiSE 2 were eligible to enter PRECiSE 3, an ongoing, open-label extension trial in which patients have received certolizumab pegol every four weeks for a total of 80 weeks. PRECiSE 3 is the first prospective trial in which patients received continuous or interrupted therapy for greater than 12 months and were not offered the option to increase their dose.

Responses at week 26 for the continuous and drug-interruption groups were 56.3 percent and 37.6 percent, respectively. Corresponding remission rates were 47.9 percent and 32.4 percent, respectively. Of patients responding at week 26, response rates at week 80 in the continuous and drug-interruption groups were 66.1 percent and 63.3 percent, respectively. Among patients in remission at week 26, week 80 remission rates were 62.1 percent and 63.2 percent, respectively. More patients in the drug-interruption group developed antibodies against certolizumab pegol and had lower plasma concentrations of certolizumab pegol than the continuously treated group.

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