Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis

Colombel JF, Rutgeerts P, Reinisch W, Esser D, Wang Y, Lang Y, Marano CW, Strauss R, Oddens BJ, Feagan BG, Hanauer SB, Lichtenstein GR, Present D, Sands BE, Sandborn WJ

Gastroenterology 2011;141:1194-201

JOHANNE BROOKS
ST3 Gastroenterology
James Paget University Hospital
Great Yarmouth
Suffolk, United Kingdom

Johanne Brooks
is a Gastroenterology Trainee in the East of England. She has an interest in the clinical impact of research on inflammatory bowel disease.

Introduction

In terms of the number of investigations into the use of biologics to induce and maintain clinical remission, Ulcerative Colitis (UC) has been a 'neglected cousin' to Crohn's Disease. ACT-1 and ACT-2 [1] assessed the efficacy and safety of infliximab versus conventional treatment in patients with moderately to severely active UC. UC patients in the infliximab arm were more likely to achieve clinical response, remission or mucosal healing at weeks 8, 30 and 54 than those receiving conventional treatment. In addition, maintenance infliximab reduced the risk of colectomy in this UC patient population [2]. Colombel et al. have undertaken a subgroup efficacy analysis of ACT-1 and ACT-2 to evaluate a possible correlation between endoscopy subscores at 8 weeks of treatment with infliximab or placebo and subsequent long-term clinical outcomes at week 54. The outcomes assessed included colectomy rates, commercial infliximab use, symptomatic remission (Mayo Stool Frequency of 0 or 1 and a rectal bleeding subscore of 0), corticosteroid-free symptomatic remission, corticosteroid-free status and sustained mucosal healing. In effect they asked the question: Does the patient's response at 8 weeks predict what will happen in a year's time?

ACT-1 and ACT-2 [1] enrolled UC patients with moderately to severely active colitis despite conventional treatment and placed them into one of three arms: placebo, infliximab (5 mg/kg) and infliximab (10 mg/kg). Colombel et al. separated each of these arms into their Mayo endoscopy subscores at week 8.

Key findings

The results at face value appear intuitive: UC patients who achieved mucosal healing (subscore 0 or 1) at 8 weeks in the infliximab arms had a lower colectomy rate ($p=0.0004$), a lower commercial infliximab use ($p < 0.0001$), an increased likelihood of being in symptomatic remission (p0.0001) and corticosteroid-free symptomatic remission ($p < 0.0001$), a reduced need for corticosteroids ($p < 0.0001$) and an increased rate of sustained mucosal healing ($p < 0.0001$) at 54 weeks. No trend towards improvement was seen in the placebo arm for the endpoints of colectomy and commercial infliximab use until 54 weeks. At 54 weeks, UC patients receiving placebo who had a low endoscopy score at week 8 were more likely to be in symptomatic remission and corticosteroid-free symptomatic remission, to be corticosteroid free and to exhibit sustained mucosal healing, though the percentages achieving these outcomes were lower compared to the infliximab-treated patients. It has to be borne in mind, however, that the numbers of patients were small, especially in the subgroup that had achieved mucosal healing at 8 weeks, and therefore caution should be exercised in interpretation of these data.

Why is this important?

Infliximab has previously been shown to improve mucosal healing in UC. This study adds support to the growing evidence that achievement of early mucosal healing may lead to improved long-term clinical outcomes. In addition, these results emphasize the value of endoscopically detected mucosal healing in predicting outcome versus facilitating the clinical response only. However, formal randomized controlled trials need to be undertaken to compare the long-term outcome in patients with symptomatic clinical remission versus mucosal healing.

ECCO editor's comment from the origianl article

"this study was designed and conducted by the ACT-1 and ACT-2 Steering Committees, Centocor Research & Development, a division of Johnson & Johnson Pharmaceutical Research & Development, LLC and Schering Corporation (a subsidiary of Merck & Co, Inc) who jointly analyzed and interpreted the data, and contributed to the manuscript"

References

1. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy of ulcerative colitis. N Engl J Med 2005;353:2462-76.
2. Sandborn WJ, Rutgeerts P, Feagan BG, et al. Colectomy rate comparison after treatment of ulcerative colitis with placebo or infliximab. Gastroenterology 2009;137:1250- 60.