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Infliximab: a new treatment for ulcerative colitis

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TITLE Infliximab for induction and maintenance therapy for ulcerative colitis

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KEYWORDS Infliximab, ulcerative colitis

LIST OF ABBREVIATIONS Acute Ulcerative Colitis Trial (ACT), number needed to treat (NNT), tuberculosis (TB), ulcerative colitis (UC)

DECLARATION OF INTERESTS Dr Andrew Williams has been in receipt of a grant from Schering-Plough UK to audit infliximab use in Crohn's disease in Scotland on behalf of the Scottish Society of Gastroenterology. He is a member of the Schering-Plough UK Ulcerative Colitis Advisory Board.

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SUMMARY

This paper presents data from two randomised multicentre studies in active UC, ACT1 (European) and ACT2 (USA). Seven hundred and twenty-eight patients with moderately active UC of mean Mayo severity score 8·4 (the maximum possible score is 12), resistant to conventional treatment (corticosteroids, immunomodulatory therapy, aminosalicylates), received placebo or infliximab infusions at zero, two and six weeks, and then every eight weeks. At eight weeks, 69·4% of patients treated with 5 mg/kg of infliximab in ACT1 and 64·5% in ACT2 showed a clinical response compared with 37% in ACT1 and 29% in ACT2 given a placebo. At 30 weeks, 52% of infliximab-treated patients in ACT1 and 47% in ACT2 maintained a response; mucosal healing occurred in 50% of ACT1 and 46% of ACT2 infliximab- treated patients. The placebo response was 25% in ACT1 patients and 30% in ACT2 patients. Twenty-six percent of infliximab-treated patients who were initially receiving corticosteroids were in remission without corticosteroids at 54 weeks (compared to 16% of placebo-treated patients).

COMMENT

These studies demonstrate that infliximab is an effective therapy in UC, although five patients need to be treated for one to benefit (NNT 5). This compares with an NNT of 3 in severe Crohn's disease and 4 in fistulising Crohn's disease. Azathioprine, in inflammatory bowel disease, has an NNT of 5.

The adverse events are similar to those reported previously. Infliximab can cause serious opportunistic infections. One patient in the infliximab-treated group developed TB, and although no deaths occurred during the trial period, one infliximab-treated patient died from histoplasmosis in a trial extention. The long-term risk of infliximab in predisposing to lymphoma and the potential to accelerate dysplasia and colorectal malignancy in UC are still concerns, although worldwide safety data are reassuring in relation to the former.

The alternative to medical treatment in UC is surgery, and the colectomy data for the ACT studies have not been presented. We do not know if infliximab response alters the natural history of UC or merely delays further relapse and requirement for surgery.

Two patient populations in UC may benefit from infliximab. The ACT studies have addressed patients with chronic active UC who are not hospitalised and who are systemically well. These patients should be considered for infliximab, but only after failure to respond to, or intolerance of, immunomodulatory therapy. The other group of patients are those with severe UC who have been hospitalised and who are being considered for emergency surgery. These patients may benefit from the infliximab as a rescue therapy, but this was not addressed in the ACT studies. Surgery is a cure for UC and should be considered in any patient not responding to medical therapy.