



Title	Systematic Review and Economic Evaluation of the Effectiveness of Infiximab for the Treatment of Crohn's Disease
Agency	NCCHTA, National Coordinating Centre for Health Technology Assessment Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom; Tel: +44 2380 595586, Fax: +44 2380 595639
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Aim

1) How effective is infiximab as second- or third-line treatment for severe active Crohn's disease in adults not responding to usual treatment? 2) How effective is infiximab at reducing the number of draining fistulae in adult patients with fistulizing Crohn's disease not responding to usual treatment? 3) What is the rate and severity of adverse effects with infiximab? 4) What adverse events are associated with repeated treatment with infiximab? 5) How cost-effective is infiximab for the above indications compared to standard practice?

Conclusions and results

Infiximab in chronic active Crohn's disease, resistant to usual treatment, was evaluated in 3 trials involving 754 patients. A single dose of infiximab showed significant benefit at week 4, with approximately 30% of patients achieving remission of symptoms. Benefit was short-lived with most patients relapsing beyond week 12. Data on repeated treatment were less clear. One trial evaluated infiximab in fistulizing Crohn's disease. A 3-dose treatment resulted in complete healing of perianal/ abdominal fistulae for more than 21 days in 46% of patients treated with infiximab vs. 13% treated with placebo. Again, benefit was short-lived, with a median duration of 3 months. For a 70 kg patient, the cost of one dose of infiximab, 5 mg/kg, is about £1800, and a 3-dose course costs about £5400. In the Schering-Plough Ltd model, the cost/QALY in treating chronic active Crohn's disease was £6700 with a single-dose treatment, £10,400 with episodic re-treatment, and £84,400 with maintenance treatment. The benefits may be overestimated due to assumptions that the drug influences the natural history of the disease. In fistulizing Crohn's disease, the cost/QALY values were high. The chronic active model was sensitive to rate of 'flare' for episodic treatment. The flare rate chosen was 10%. If more frequent flare was seen, then costs increased substantially. The fistulizing model was relatively insensitive to costs offset, even when assuming 100% offset.

Recommendations

Infiximab is a specialized treatment requiring intravenous administration. Patients considered for infiximab treatment must be fully assessed by specialists experienced in managing severe Crohn's disease. These patients will have disease that is not amenable to conventional medical and surgical management. Use of infiximab is likely to be limited to a small group of patients, in whom benefits over existing treatment can be expected.

Methods

RCTs addressing the above issues were systematically reviewed. The economic evaluation submitted by Schering-Plough Ltd was critiqued and the cost/quality-adjusted life-year (QALY) re-estimated by adjusting the assumptions.

Further research/reviews required

Further research is needed in this rapidly developing field. Research needs to clarify optimal dosage and dosage frequency for infiximab, the characteristics of poorly responding patients, and its optimal place in therapy among the other treatment options, including surgery.