Review: Infliximab increases response and remission rates in fistulizing or treatment-resistant Crohn disease

Marshall JK, Blackhouse G, Goeree R, et al. **Infliximab for the treatment of Crohn's disease: a systematic review and cost-utility analysis.** Technology report no. 24. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2002. www.ccohta.ca.

QUESTION

In patients with fistulizing or treatment-resistant Crohn disease, is infliximab safe and effective?

DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, Current Contents, CINAHL, HealthSTAR, TOXLINE, the Cochrane Library, Drug Info Full Text, Pharmaceutical & Health Care Industry News, PharmaProjects, and Pharmaceutical News Index (1990 to May 2001). Scientific meeting abstracts were searched; major clinical gastroenterology journals were hand searched (to August 2001); and authors, government agencies, and pharmaceutical companies were contacted.

STUDY SELECTION

2 reviewers independently selected English-language randomized controlled trials (RCTs) that reported clinical end points for infliximab treatment in adults with fistulizing or treatment-resistant Crohn disease.

DATA EXTRACTION

2 independent reviewers extracted data on study centers, source of funding, patients, treatment regimens, quality of study methods, and outcomes (response, remission, and fistula closure).

MAIN RESULTS

4 RCTs met the selection criteria. *Fistulizing Crohn disease:* 1 RCT (n = 94) showed that more patients in the infliximab groups than in the placebo group had ≥ 50% closure (Table). *Treatment-resistant Crohn disease:* RCTs of treatment-resistant Crohn disease were too heterogeneous to be combined. The Table shows the 4-week and 12-week results for 1 RCT (n = 108); in responders, reinfusions of 10-mg infliximab at 8-week intervals led to more remissions (44% vs 20%, P = 0.013) at 44 weeks than did placebo, but the difference in response rate was not statistically significant (62% vs 37%, P = 0.16).

The interim 30-week results for 1 RCT (n = 335) still in progress showed a benefit for maintenance 5-mg or 10-mg infliximab (Table). Data from controlled clinical trials showed that serious adverse events occurred in 13% of patients treated with infliximab and 4% of patients treated with placebo.

CONCLUSION

In patients with fistulizing or treatment-resistant Crohn disease, infliximab increases remission and response rates.

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For correspondence: Dr. J.K. Marshall, McMaster University, Hamilton, Ontario, Canada. E-mail marshallj@mcmaster.ca.

Infliximab (inflix) for Crohn disease (CD)*

Patient group	Outcomes	Number of patients	Dose	Inflix	Placebo	RBI (95% CI)	NNT (CI)
Fistulizing CD	≥ 50% closure at 18 wk	94	5 mg, 10 mg	62%	26%	140% (37 to 363)	3 (2 to 7)
Treatment-resistant CD	Response at 4 wk	108	5 mg, 10 mg, 20 mg	65%	16%	307% (84 to 928)	3 (2 to 4)
	Response at 12 wk	108	5 mg, 10 mg, 20 mg	41%	12%	241% (31 to 908)	3 (2 to 12)
	Remission at 12 wk	108	5 mg, 10 mg, 20 mg	24%	8.0%	201% (–10 to 10)	Not significant
			Repeat doses Single dose				
	Response at 30 wk†	335	5 mg, 10 mg vs 5 mg	55%	27%	102% (48 to 183)	4 (3 to 6)
	Remission at 30 wk†	335	5 mg, 10 mg vs 5 mg	42%	21%	100% (37 to 199)	5 (4 to 10)

*Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.
†Interim data reported from a 102-week ongoing trial of maintenance infliximab.

COMMENTARY

Marshall and colleagues have systematically reviewed the new, interesting topic of treating Crohn disease with infliximab (a chimeric human–murine monoclonal antibody against the proinflammatory cytokine tumor-necrosis factor–α) and the economic effect of this treatment. The percentage of improvement in patients who received infliximab in all of the studies is impressive, and no doubts exist about its effectiveness in either fistulizing or refractory disease. A recent trial by Hanauer and colleagues (1) also encourages use of this drug for inducing and maintaining clinical remission in patients with Crohn disease. The high cost of the treatment might be balanced, at least in part, by a substantial improvement in the quality of life of the patients.

The trials on infliximab suggest that large, serious, and rarely life-threatening side effects, such as acute infusion reactions, human antichimeric antibodies, autoimmune disorders, malignancy, and infection (i.e., tuberculosis and intestinal strictures), may result from this treatment. A causal association for some of these side effects is not established yet, but no doubt exists that this very potent drug must be managed with great care. The long-term follow-up will help us better understand the potential and proper use of this new agent. In the meantime, treatment with infliximab should be offered to a select subgroup of patients with Crohn disease in whom the need of more effective treatment for severe, persevering, and life-limiting symptoms is balanced with the risk for potentially serious side effects.

Andrea Belluzzi, MD
S. Orsola Hospital
Bologna, Italy

Reference

1. **Hanauer SB, Feagan BG, Lichtenstein GR, et al, for the ACCENT I Study Group.** Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002;359:1541-49.

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