Efficacy and safety of certolizumab pegol for Crohn's disease: a systematic review and meta-analysis
Da W, Zhu J, Wang L, Lu Y

CRD summary
This review suggested that certolizumab may be an effective and safe maintenance therapy drug for Crohn's disease (chronic inflammatory condition of the gut), but further high-quality studies were needed to confirm these findings and assess the role of the drug in induction therapy. Despite some limitations of the review, the authors' conclusions appear to be reliable.

Authors' objectives
To examine the efficacy and safety (side effects) of certolizumab pegol as induction and maintenance therapy for Crohn's disease

Searching
MEDLINE, BioMed Central, China National Knowledge Infrastructure (CNKI), and The Cochrane Library were searched from January 1980 to December 2011. Search terms were reported. Google Scholar, the Directory of Open Access Journals, meta-analyses and guidelines were also searched.

Study selection
To be eligible for the review, studies had to be randomised controlled trials (RCTs) of the efficacy of certolizumab in patients with Crohn's disease.

All included trials were randomised and placebo-controlled. Both induction and maintenance therapy trials were included. The timing of assessment in the induction trials ranged from week four to week 12 and week 26 in the maintenance trials. Patients had moderate to severe Crohn's disease.

It appeared that two reviewers were involved in selecting studies for the review, with disagreements resolved by another reviewer.

Assessment of study quality
Trial quality assessment was performed using the Jadad scale of five questions based on randomisation, blinding and drop-outs.

It appeared that two reviewers were involved in trial quality assessment, with disagreements resolved by another reviewer.

Data extraction
Response rates and remission rates were used to evaluate treatment efficacy. Treatment-related toxicity was used to evaluate safety. Odds ratios with 95% confidence intervals were calculated for these outcomes.

Two independent reviewers extracted data from the studies, with any disagreements resolved by a third reviewer.

Methods of synthesis
Heterogeneity was assessed using the Q statistic and I². If heterogeneity was found, a random-effects model of meta-analysis was used; otherwise, a fixed-effect model was used. Pooled odds ratios were calculated.

Subgroup analyses of efficacy and safety were conducted according by therapy (induction or maintenance) using fixed-effect models.

Publication bias was assessed using funnel plots for the outcomes of response, remission and treatment-related toxicity rates. Fail-safe N statistics and Egger's test were also used to assess publication bias.
Results of the review

Five RCTs (1,891 participants, range 92 to 659) were included in the review. All trials scored 3 or more points (out of 5) on the quality scale.

Response rates across the trials ranged from 23% to 63% for certolizumab and from 16% to 56% for placebo. Remission rates ranged from 14 to 48% for certolizumab and from 10% to 29% for placebo. Treatment-related toxicity rate ranged from 18.4% to 43.4% for certolizumab and from 13.5% to 42.5% for placebo.

Certolizumab significantly increased overall response rate compared with placebo (OR 1.565, 95% CI 1.056 to 2.321; I²=69.9%; high heterogeneity analysis using random-effects model). Certolizumab significantly increased overall remission rate compared with placebo (OR 1.626, 95% CI 1.297 to 2.038; I²=26.5%; low heterogeneity analysis using fixed-effect model). Certolizumab did not significantly increase treatment-related toxicity rate compared with placebo (OR 0.985, 95% CI: 0.799 to 1.214; I²=17%; fixed-effect model).

Subgroup analyses showed that maintenance therapy (but not induction therapy) significantly increased response rate and remission rate compared with placebo. Neither induction nor maintenance therapy increased treatment-related toxicity rate. Full results of subgroup analyses were reported in the paper.

There was no significant evidence of publication bias.

Authors' conclusions

Certolizumab may be effective as a maintenance therapy for Crohn's disease and appeared to have a favourable safety profile; further high-quality studies were necessary to confirm the findings of this review and to assess the role of the drug in induction therapy.

CRD commentary

This review had a defined question and was underpinned by a search of several databases and sources. Two major databases (EMBASE and CINAHL) were not searched, which the authors acknowledged as a limitation of the review. Papers published in languages other than English were not sought, which meant that studies may have been missed. One RCT was excluded as it was not placebo controlled, but this was not a predefined inclusion criterion. Assessment of publication bias suggested a large number of studies would be needed to overturn any conclusions but as only five trials were included in the review, this assessment may not be reliable.

Trial quality was assessed, but the tool used was quite limited and overall scores not recommended. Further trial details on the participants would have been helpful. The meta-analysis was appropriate but did show a high degree of heterogeneity in some analyses which was not fully explored by the authors. Subgroup analyses were based on only two or three trials.

Despite some limitations of the review, the authors' overall conclusions appear to be reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice

Research: The authors stated that further high quality RCTs were necessary to confirm the findings of this review and to assess the role of the drug in induction therapy for Crohn's disease. Further trials were also needed to assess long-term efficacy and safety of certolizumab and to compare it with other TNF-alpha antagonists and other medications used to treat Crohn's disease.

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Bibliographic details


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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.