Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials

Reich K, Burden AD, Eaton JN, Hawkins NS

CRD summary
The authors concluded that infliximab was the most effective treatment for moderate to severe psoriasis, followed by ustekinumab, adalimumab, etanercept and efalizumab. The review was generally well conducted. Only short-term outcomes were analysed, so the long-term effects of the treatments was not known. Apart from this, the results of the review are likely to be reliable.

Authors' objectives
To compare the effectiveness of all currently available biologic agents for the treatment of moderate to severe psoriasis.

Searching
MEDLINE and EMBASE were searched from January 1995 to October 2008. The Cochrane Library was also searched. Reference lists of included studies were checked. Abstracts from major dermatology meetings were searched to identify unpublished studies.

Study selection
Randomised controlled trials for treatment of plaque-type psoriasis in adults were eligible. Trials had to be placebo controlled or head-to-head comparisons of monotherapy. Eligible treatments were adalimumab, efalizumab, etanercept, infliximab, and ustekinumab. All treatments had to be given at the approved dose.

Most included trials were of 12 weeks duration (range 10 to 30 weeks). Disease severity was similar across trials; mean duration of disease was 18 to 22 years. Most patients had received prior systemic or phototherapy treatment. The mean age of patients ranged from 44 to 47 years; 60 to 70% were men. Most patients were Caucasian.

Study selection was performed by two reviewers.

Assessment of study quality
The Jadad scale was used to assess trial quality.

The number of reviewers that assessed quality was not reported.

Data extraction
Data were extracted on the Psoriasis Area and Severity Index (PASI) for each arm of each trial. Numbers of patients at the PASI 50, PASI 75 and PASI 90 levels were extracted.

The number of reviewers that performed the data extraction was not reported.

Methods of synthesis
A network meta-analysis was used to compare treatments of PASI 50, 75 and 90 response rates. A Bayesian analysis was performed using the WinBUGS software. Some technical details of the analysis process and priors used were reported. The analysis was performed on a probit scale, with results converted into relative risks (RR) of the effect of each treatment compared with placebo, with 95% credible intervals (95% CrI). A sensitivity analysis to account for the different recommended doses of ustekinumab depending on patient weight was performed.

Results of the review
Twenty trials, with over 10,000 patients, were included in the review; sample sizes ranged from 22 to 1,230 patients. There were three trials of adalimumab, five of efalizumab, five of etanercept, four of infliximab, and three of ustekinumab; only one trial was a comparison of treatments, the rest were placebo controlled. All trials were of high quality (Jadad scores ranged from 3 to 5).
For the PASI 50 (Psoriasis Area and Severity Index 50%) outcome, infliximab was found to be the most effective treatment when compared with placebo (RR 7.3, 95% CrI 6.6 to 8.1). This was followed by ustekinumab 90mg (RR 7.1, 95% CrI 6.5 to 7.8), adalimumab (RR 6.4, 95% CrI 5.7 to 7.1), etanercept 50mg (RR 6.0, 95% CrI 5.4 to 6.6), and efalizumab (RR 4.0, 95% CrI 3.5 to 4.5). The ordering of treatments was the same for the PASI 75 and PASI 90 outcomes. There was a 93% probability that infliximab was the most effective treatment.

Authors' conclusions
Infliximab was the most effective treatment for psoriasis, followed by ustekinumab, adalimumab, etanercept and efalizumab (in descending effectiveness order).

CRD commentary
This appeared to be a well conducted review, although reporting of some aspects of the review process was limited. The search was appropriate; an effort was made to identify all relevant trials including unpublished trials. The authors sought to avoid potential reviewer biases in the study selection process.

Study quality was assessed and all included studies were judged to be of high quality. Suitable statistical methods were used to combine trials. A large number of trials and patients were included. The authors noted that there were no head-to-head comparisons of treatments, so direct comparison of treatments was not possible. They also noted that the outcome considered was short-term, and that the longer-term effects of the treatments were not known.

Apart from the above concerns, the results of the review are likely 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 research was needed to compare treatments after long-term follow-up.

Funding
Janssen-Cilag Ltd.

Bibliographic details

PubMedID
21910698

DOI
10.1111/j.1365-2133.2011.10583.x

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Adalimumab; Adult; Antibodies, Monoclonal /therapeutic use; Antibodies, Monoclonal, Humanized /therapeutic use; Biological Products /therapeutic use; Dermatologic Agents /therapeutic use; Etanercept; Female; Humans; Immunoglobulin G /therapeutic use; Infliximab; Male; Middle Aged; Psoriasis /drug therapy; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Treatment Outcome; Ustekinumab

AccessionNumber
12012002139
Date bibliographic record published
25/04/2012

Date abstract record published
11/10/2012

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.