Comparative effects of biological therapies on the severity of skin symptoms and health-related quality of life in patients with plaque-type psoriasis: a meta-analysis

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CRD summary
This review found that active treatment with biological response modulator therapy significantly reduced the severity of skin disease and improved quality of life in patients with moderate to severe chronic plaque-type psoriasis. Lack of information about the included patients, trial quality and poor reporting of the review process means that the reliability of the authors’ conclusions is unclear.

Authors' objectives
To evaluate the safety and effects of biological response modulators on the severity of psoriasis and on quality of life.

Searching
MEDLINE, EMBASE, the Cochrane Central Register of Controlled trials (CENTRAL) and the Cochrane Database of Systematic Reviews were searched from inception to December 2006 to identify relevant studies; search terms were reported. Reference lists of retrieved studies, pertinent reviews and a previous HTA report were scanned to identify additional studies. There were no language restrictions.

Study selection
Randomised controlled trials (RCTs) that evaluated the use of the biological response modulators (alefacept, efalizumab, infliximab or etanercept) in patients with moderate to severe psoriasis. Trials had to report the use of licensed doses of each of the medications and have duration of 10 weeks or longer to be included in the meta-analysis. Trials reported only as abstracts were included if sufficient information was provided in the abstract.

All the included RCTs were placebo-controlled. There were no direct comparisons made between biological response modulator therapies in included trials. The biological response modulators included alefacept, efalizumab, etanercept and infliximab, given at a range of doses. The patients in almost all the trials had clinically stable but active psoriasis of more than 10% of body surface area; in one trial patients were included if psoriasis affected 5% or more of body surface area. The mean duration of psoriasis ranged between 16 and 23 years.

The primary outcomes were the attainment of a 75% reduction from a baseline score on the Psoriasis Area and Severity Index (PASI 75) and health-related quality of life according to data from the Dermatology Life Quality Index. Similar analyses were conducted for patients attaining reductions from baseline levels by 50% (PASI 50) and 90% (PASI 90). Safety data pertaining to treatment discontinuation were also evaluated. Mean baseline PASI across the trials ranged between 17 to 34%.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The authors did not state they assessed methodological quality.

Data extraction
Data were extracted to calculate relative risks (RRs) and corresponding 95% confidence intervals (CIs) for each biological response modulator compared with placebo where patients achieved 75% reductions in baseline scores on the PASI 75, with similar analyses undertaken for patients achieving a PASI 50 and PASI 90. Mean differences (MDs) from baseline Dermatology Life Quality Index scores were calculated. The numbers of patients who discontinued treatment with biological response modulators were tabulated.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated using a Mantel-Haenszel fixed-effect model for the PASI 75, PASI 50 and PASI 90. Statistical heterogeneity was evaluated using Cochran's Q-statistic. In the event of statistical heterogeneity, a random-effects model was used. The pooled mean differences in Dermatology Life Quality Index scores and 95% confidence intervals between each biological response modulator and placebo were also calculated. An ordered-probit model was used because of the indirect comparisons used in the review.

**Results of the review**

Fifteen RCTs were included in the meta-analysis (6,973 patients; appendix 2). A further eight trials appear to have been included in the quality of life analysis (table 5). The follow-up time used in the meta-analyses was after 10 to 12 weeks of treatment.

**Psoriasis severity outcomes:** Compared with placebo, statistically significant benefits were observed in attaining a 75% reduction from baseline in the Psoriasis Area and Severity Index (PASI 75) with biological therapy using infliximab (RR 25.48, 95% CI 14.04 to 46.23; four RCTs n=1,072 patients), etanercept 50mg/kg administered subcutaneously twice weekly (RR 11.92, 95% CI 8.17 to 17.39, three RCTs; n=1,334 patients), etanercept 25mg/kg administered subcutaneously twice weekly (RR 10.68, 95% CI 6.15 to 18.57; three RCT), efalizumab 1 to 2mg/week (RR 7.47, 95% CI 5.20 to 10.73; four RCTs), and alefacept administered weekly at a range of doses (RR 3.37, 95% CI 2.18 to 5.23; three RCTs). Findings were similar for the proportions of patients achieving PASI 50 and PASI 90.

The results from the hierarchical model indicated that the use of infliximab significantly increased the likelihood of patients attaining a PASI 50, PASI 75 or a PASI 90 response at 10-12 weeks of follow-up compared to both dose of etanercept, efalizumab, and alefacept.

Statistically significant heterogeneity was observed only for the comparison of infliximab with placebo for the proportions of patients attaining PASI 50 (Q=4.77, p=0.029) and PASI 75 (Q=8.742, p=0.033).

**Quality of life outcomes:** Compared with placebo, statistically significant benefits were achieved in health-related quality of life measured by the Dermatology Life Quality Index with biological therapy using infliximab 5mg/kg (pooled MD 8.52, 95% CI 4.95 to 12.08; two RCTs), etanercept 50mg twice weekly (pooled MD 6.07, 95% CI 3.99 to 8.16; three RCTs), etanercept 25mg twice weekly (pooled MD 5.66, 95% CI 3.27 to 8.04; two RCTs), efalizumab (pooled MD 3.54, 95% CI 2.05 to 5.02; two RCTs), and alefacept (pooled MD 1.65, 95% CI 1.23 to 2.07, six trials).

**Safety:** There were no differences in the proportions of patients who discontinued treatment between the biological response modulator treatment groups and the patients who received placebo treatment.

**Authors' conclusions**

Infliximab significantly reduced the severity of psoriasis compared with placebo in patients with moderate to severe psoriasis. All the biological response modulator therapies included in the trials improved health-related quality of life compared with placebo in these patients. There were no observed differences in the proportions of patients who discontinued treatment. Toxicity profiles were not examined; head-to-head comparisons of different medications were recommended.

**CRD commentary**

The review addressed a clear question and criteria for the inclusion of studies were stipulated. Appropriate databases were searched with no any language restrictions. There were attempts to identify unpublished studies, which reduced the risk of publication bias. Measures to minimise errors and bias were not reported for any part of the review process.

There was no assessment of methodological quality, so the reliability of the included trials was unknown. Pooling of the trial results appeared to be justified. There was a lack of information on the patient population included in the trials.

The uncertain quality of the included trials and poor reporting of the review process mean the reliability of the authors' conclusions is unclear.

Five of the authors disclosed financial links with various pharmaceutical companies (including the manufacturers of some of the drugs assessed in this review).
Implications of the review for practice and research

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that the findings of this review should be further investigated in randomised controlled trials in which active treatments are compared to further determine the most effective treatment.

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