Title **The Clinical and Cost Effectiveness of Anakinra for the Treatment of Rheumatoid Arthritis in Adults: A Systematic Review and Economic Analysis**

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Reference Health Technol Assess 2004;8(18). May 2004. www.ncchta.org/execsumm/summ818.htm

Aim

To review the evidence of the clinical and cost effectiveness of anakinra, an interleukin-1 receptor antagonist (IL-1Ra), in treating rheumatoid arthritis (RA) in adults.

Conclusions and results

Five high-quality randomized controlled trials (RCTs) of anakinra in adult RA patients were identified. Results of the clinical trials were consistent with clinical benefit as measured by the American College of Rheumatology (ACR) composite response rate at 6 months. Response rates varied across the trials, which may reflect the size of the trials and the range of doses evaluated. Consistent benefit was seen at the higher dose. Benefit was evident with monotherapy and in combination with methotrexate. Data on the efficacy endpoints in a large pragmatic safety study have not been made available, which is of concern. Anakinra was associated with a high incidence of injection-site reactions. Serious adverse events were infrequent, but longer term followup is required. No published economic evaluations of anakinra in RA patients were identified. The Birmingham Rheumatoid Arthritis Model (BRAM) gives a base-case estimate of the incremental cost-effectiveness ratio (ICER) of anakinra of £106,000 to £604,000/quality-adjusted life-year (QALY). Substantial variations were made in key parameters in sensitivity analyses. ICERs were responsive, but did not drop below £50,000/QALY in any univariate sensitivity analysis.

Recommendations

Based on ACR response, anakinra is modestly effective in treating RA, but no conclusions can be drawn on the effect of treatment on disease progression. Adjusted indirect comparison suggests that anakinra may be significantly less effective at relieving the clinical signs and symptoms of RA than tumor necrosis factor (TNF) inhibitors used in combination with methotrexate, but these results should be interpreted with caution. BRAM produces an ICER for anakinra substantially higher than those for infliximab and etanercept. However, patients may respond to anakinra when they have not responded to other TNF inhibitors. Anakinra may yield a clinically significant improvement in some patients that could not otherwise be achieved.

Methods

Studies were identified that included RCTs or economic evaluations of anakinra in adult patients with RA. Health economic reviews were assessed. Data were extracted and quality assessed using a structured approach. BRAM was used to compare disease-modifying antirheumatic drug (DMARD) sequences chosen to reflect current clinical practice, with and without anakinra, at different points in the DMARD sequence.

Further research/reviews required

RCTs to evaluate the efficacy, safety, and cost of anakinra over the longer term. Comparative trials of anakinra with other DMARDs and biological modifiers. Assessment of anakinra in treating patients who failed to achieve benefit while taking infliximab or etanercept. Assessment of the impact of DMARDs and anakinra on joint replacement, mortality, and quality of life. Controlled clinical trials of combination therapy with two anticytokines. Investigation of newer biological therapies. Utility of radiographic outcomes in clinical trials of RA.

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