INAHTA Briefs

Issue 2007/71

Title **A Systematic Review of the Effectiveness of Adalimumab, Etanercept, and Infliximab for the Treatment of Rheumatoid Arthritis in Adults and an Economic Evaluation of their Cost Effectiveness**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2006;10(42). Nov 2006. www.hta.ac.uk/execsumm/summ1042.htm

Aim

To review the clinical and cost effectiveness of adalimumab, etanercept, and infliximab – agents that inhibit tumor necrosis factor-alpha (TNF-alpha) – in treating rheumatoid arthritis (RA) in adults.

Conclusions and results

Twenty-nine randomized controlled trials (RCTs), most of high quality, were included. The only head-to-head comparisons were against methotrexate. In patients with short disease duration who were naïve to methotrexate, adalimumab was marginally less and etanercept was marginally more effective than methotrexate in reducing symptoms of RA. Etanercept was better tolerated than methotrexate. Both adalimumab and etanercept were more effective than methotrexate in slowing radiographic joint damage. Etanercept was also marginally more effective and better tolerated than methotrexate in patients with longer disease durations who had not failed methotrexate treatment. Infliximab is only licensed for use with methotrexate. All 3 agents, alone or in combination with ongoing disease-modifying antirheumatic drugs (DMARDs), were effective in reducing symptoms and signs of RA in patients with established disease. In patients who were naïve to methotrexate, or who had not previously failed methotrexate treatment, a TNF inhibitor combined with methotrexate was significantly more effective than methotrexate alone. Infliximab combined with methotrexate increased the risk of serious infections. All 10 published economic evaluations met standard criteria for quality, but the incremental cost-effectiveness ratios (ICERs) were very high in some instances. For use in accordance with NICE guidance as the third in a sequence of DMARDs, the base-case ICER was around GBP 30 000 per QALY in early RA and GBP 50 000 per QALY in late RA. TNF inhibitors are most cost effective when used last. The ICER for etanercept used last is GBP 24 000 per QALY, substantially lower than for adalimumab or infliximab. First line use as monotherapy generates ICERs around GBP 50 000 per QALY for adalimumab and etanercept. Using the combination of methotrexate and a TNF inhibitor as first line treatment generates much higher ICERs, as it precludes subsequent use of methotrexate, which is cheap. The ICERs for sequential use are of the same order as using the TNF inhibitor alone.

Recommendations

Adalimumab, etanercept, and infliximab are effective treatments compared with placebo for RA patients who are not well controlled by conventional DMARDs. The combination of a TNF inhibitor with methotrexate was more effective than methotrexate alone in early RA, but clinical relevance of this additional benefit is yet to be established. An increased risk of serious infection cannot be ruled out in combining methotrexate with adalimumab or infliximab. TNF inhibitors are most cost effective when used as last active therapy. In this analysis, other things being equal, etanercept may be the TNF inhibitor of choice, but this may depend on patient preference as to route of administration. The next most cost-effective use of TNF inhibitors is third line, as recommended in the 2002 NICE guidance.

Methods

Systematic reviews of the literature on effectiveness and cost effectiveness were undertaken. Many databases were searched up to February 2005, information was sought from researchers and industry, and industry submissions to NICE were reviewed. Meta-analyses of effectiveness data were undertaken for each agent. A simulation model (BRAM) was further developed and used to produce an incremental cost-effectiveness analysis.

Further research/reviews required

Direct comparative RCTs of TNF inhibitors against each other and against other DMARDs, and sequential use in patients who have failed a previous TNF inhibitor, are needed. Longer-term studies of the quality of life in patients with RA and the impact of DMARDs on this are needed, as are longer studies that directly assess effects on joint replacement, other morbidity, and mortality.

Written by Dr Amanda Burls, University of Birmingham, United Kingdom

ISSN 1654-501X