UK cost-utility analysis of rituximab in patients with rheumatoid arthritis that failed to respond adequately to a biologic disease-modifying antirheumatic drug

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study evaluated the cost-effectiveness of rituximab for patients with rheumatoid arthritis which had failed to respond to biological disease modifying antirheumatic drugs. The authors concluded that the addition of rituximab was cost-effective compared with standard care alone. Overall, the level of reporting was good and the quality of the study was satisfactory. The authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The aim of the trial was to evaluate the cost-effectiveness of rituximab in patients with rheumatoid arthritis, which had failed to respond to two non-biological disease modifying antirheumatic drugs (nbDMARDs) and one tumour necrosis factor (TNF) inhibitor.

Interventions
This study evaluated the recommended treatment sequence, which comprised leflunomide, gold, ciclosporin, and palliative care, compared with the same sequence plus rituximab, which was incorporated as a first-line treatment. A further treatment sequence, which reflected a practice for some physicians, who switched between anti-TNF drugs, was also evaluated. This sequence comprised adalimumab, infliximab, leflunomide, gold, ciclosporin, and palliative care. This was compared with the same sequence plus rituximab as a first-line treatment.

Location/setting
UK/primary care.

Methods
Analytical approach:
This economic evaluation used a Markov model to simulate the costs and efficacy of the alternative options over the lifetime of each patient, using a six-month cycle. The authors stated that they adopted the perspectives of the National Health Service (NHS) and Personal Social Services in England and Wales.

Effectiveness data:
The clinical data were derived from a selection of relevant studies. The patients’ characteristics on entering the model were based on the Randomised Evaluation of Long-term Efficacy of rituximab in Rheumatoid Arthritis (REFLEX) trial (Cohen, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The treatment response rates were based on an indirect comparison of American College of Rheumatology (ACR) response rates compared with placebo. The ACR response rates were derived from multiple published studies (Cohen, et al. 2006, Keystone, et al. 2004, Maini, et al. 1999, see ‘Other Publications of Related Interest’ below for bibliographic details). The mortalities were based on the all cause mortality from a national database, adjusted with an rheumatoid arthritis risk multiplier, which was related to Health Assessment Questionnaire (HAQ) scores.

Monetary benefit and utility valuations:
The utility measures were derived from the HAQ scores using a published equation (Bansback, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details).

Measure of benefit:
The main benefit measure was quality-adjusted life-years (QALYs), which were discounted at 3.5% per year. Life-years gained and life expectancy were also measured.

Cost data:
The drug costs were derived from the British National Formulary (BNF) and calculated according to their licensed dosing. The required attendance time by personnel was based on a published study (Nuijten, et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details). The personnel salaries were based on Personal Social Services Research Unit (PSSRU) 2004 data. The monitoring costs were derived from the BNF, PSSRU or a published study (Barton, et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). The frequency of monitoring was based on each product summary information modified by expert opinion. The resource use data for in-patient visits came from a UK registry. The currency was UK pounds sterling (£) and the price year was not stated. An annual discount rate of 3.5% was applied to future costs.

Analysis of uncertainty:
Probabilistic sensitivity analysis was used to explore the uncertainty around the parameters. In addition, one- way analysis was used to assess the impact of the time on medication, rebound effect, utility equation, dosing frequency, HAQ score long-term deterioration on medication, and response rates on the results.

Results
For the primary analysis the total discounted QALYs were 2.324 for the standard sequence compared with 3.051 for this sequence plus rituximab, which was an incremental QALY gain of 0.727. The total direct medical costs were £30,554 for the standard sequence compared with £41,229 for this sequence plus rituximab.

This equated to an incremental cost-effectiveness ratio of £14,690 for the primary analysis.

For the secondary analysis, which assumed some switching between anti-TNF drugs, the total discounted QALYs for the standard sequence were 3.407 compared with 3.933 for this sequence plus rituximab, which was an incremental QALY gain of 0.526. The total direct medical costs were £60,480 for the standard sequence compared with £66,583 for this sequence plus rituximab.

This equated to an incremental cost-effectiveness ratio of £11,601 for the secondary analysis.

The probabilistic sensitivity analysis found that, at a threshold of $30,000, there was an 89% probability of rituximab being cost-effective.

Authors' conclusions
The authors concluded that rituximab was a cost-effective option in patients with rheumatoid arthritis, which failed to respond to nbDMARDs.

CRD commentary
Interventions:
The alternative interventions were clearly described and included the current practice in the UK setting.

Effectiveness/benefits:
The clinical estimates were derived from several published studies. The methodologies of these studies were not described in detail and an assessment of their validity was not possible. No details of how the studies were sought or selected were reported and no systematic review was reported. Therefore, it is not possible to ascertain if the best available evidence was used. The utilities were mapped from the main outcome measure (HAQ) which was disease specific. The mapping was done using a well established method, the details of which were reported.
Costs:
The methodology used to calculate the costs was described in detail. The sources of the cost data were reported, but there was no breakdown of the unit costs and quantities. Discounting was relevant and carried out in accordance with published guidelines.

Analysis and results:
The patterns of transition between health states, together with other features of the model were described in detail. An incremental analysis was appropriately conducted and the issue of uncertainty was addressed through probabilistic sensitivity analysis. The results of which were presented clearly and in full. The authors noted and discussed some limitations of their analysis such as the use of HAQ scores to predict the utilities and the heterogeneity among the sources of data. Overall the analysis was well reported.

Concluding remarks:
Overall, the level of reporting was good and the quality of the study was satisfactory. The authors’ conclusions appear to be appropriate.

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Other publications of related interest


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