Cost-effectiveness of adalimumab, etanercept, and tocilizumab as first-line treatments for moderate-to-severe rheumatoid arthritis

Soini EJ, Hallinen TA, Puolakka K, Vihervaara V, Kauppi MJ

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
The objective was to assess the cost-utility of adalimumab, etanercept, and tocilizumab, as first biologic treatments for moderate-to-severe rheumatoid arthritis, after the failure of one or more traditional disease-modifying antirheumatic drug. The authors concluded that tocilizumab with methotrexate was cost-effective. The methods were good, and they and the results were well presented. Given the scope of the study, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-utility of adalimumab, etanercept, and tocilizumab, as first biologic treatments for moderate-to-severe rheumatoid arthritis, after the failure of one or more traditional disease-modifying antirheumatic drug.

Interventions
The biologic treatments were: adalimumab with methotrexate; etanercept with methotrexate; and tocilizumab with methotrexate. These were followed by rituximab with methotrexate, then infliximab with methotrexate, and then best supportive care, which included leflunomide, then cyclosporine, then methotrexate. These interventions were compared with methotrexate alone.

Location/setting
Finland/secondary care.

Methods
Analytical approach:
A probabilistic individual-patient sampling model was used to assess the costs and outcomes of each of the interventions. The time horizon was the lifetime of the patient. The authors reported that the two perspectives were those of a health care payer and society.

Effectiveness data:
The clinical and effectiveness data were from published studies, reports, and national statistics. The main measure of effectiveness was the American College of Rheumatology (ACR) response rate, which was from a published mixed-treatment comparison, as there were no head-to-head clinical data. The response to treatment was assumed to have an impact on disease severity, which was measured by the patients’ Health Assessment Questionnaire (HAQ) scores.

Monetary benefit and utility valuations:
The utility estimates were estimated using a study of the association between HAQ score and the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) gained were the measure of benefit, and future benefits over a lifetime were discounted at an annual rate of 3%.
Cost data:
The direct costs were those of the drugs, drug administration, monitoring, and hospitalisation. Hospitalisation costs were from a published Swedish study. All other health care costs were from Finnish settings. Productivity losses were obtained from a Swedish study and valued using Finnish annual wages. All costs were updated to 2010 prices, using official Finnish health care price indices. Future costs were discounted at an annual rate of 3%. All costs were reported in Euros (EUR).

Analysis of uncertainty:
One-way sensitivity analyses were undertaken by varying the values for the model inputs. A probabilistic sensitivity analysis was undertaken by fitting probability distributions to all the model parameters; the outcomes of 3,000 patients were assessed, in 1,000 simulations. The results were presented in cost-effectiveness acceptability curves. The authors estimated the multinomial expected value of perfect information.

Results
From a societal perspective, the average cost per patient was EUR 111,927 with methotrexate alone, EUR 190,184 with etanercept, EUR 192,373 with adalimumab, and EUR 183,633 with tocilizumab (using its wholesale price). The average QALYs gained were 5.83 with methotrexate, EUR 9.52 with etanercept, 9.52 with adalimumab, and 10.03 with tocilizumab.

Compared with methotrexate alone, the incremental cost-utility ratio was EUR 21,257 per QALY gained for etanercept, EUR 21,852 per QALY gained for adalimumab, and EUR 17,091 per QALY gained for tocilizumab. Tocilizumab was dominant over etanercept and adalimumab, as it was less costly and more effective.

The probabilistic sensitivity analysis showed that at a willingness-to-pay threshold of EUR 20,000 per QALY gained, tocilizumab with methotrexate was cost-effective in 93.4% of simulations, and at EUR 25,000 per QALY gained it was cost-effective in 98.7% of simulations.

Authors’ conclusions
The authors concluded that tocilizumab with methotrexate was cost-effective for moderate-to-severe rheumatoid arthritis, after the failure of one or more traditional disease-modifying antirheumatic drugs.

CRD commentary
Interventions:
The interventions were reported appropriately. The comparators were relevant and included the most commonly used drug, adalimumab. The authors did not state that they included the most cost-effective option in their analysis.

Effectiveness/benefits:
The clinical and effectiveness evidence was from a number of different sources. The sources for the main effectiveness estimates were described, but the methods used to identify them, such as a systematic review, were not reported. As a result, it is not possible to determine if all the relevant evidence was included.

Costs:
The perspectives were explicitly reported and all the major relevant cost categories and costs, for both the health care payer and the societal perspective, appear to have been included. The sources for these costs were adequately reported. The price year, time horizon, discount rate, and currency were reported.

Analysis and results:
The cost and outcome information were combined using a probabilistic individual sampling model. The model structure was described and a diagram was given. The impact of uncertainty, on the model's results, was exhaustively tested in one-way sensitivity analyses, probabilistic sensitivity analysis, and value of information analysis. As the main limitation to their study, the authors reported that the effectiveness evidence was from an indirect comparison of treatments, rather than from head-to-head trials.

Concluding remarks:
The methods were good, and they and the results were well presented. Given the scope of the study, the authors’
conclusions appear to be valid.

**Funding**
Supported by Roche Oy, Finland, manufacturer of tocilizumab.

**Bibliographic details**

**PubMedID**
22168785

**DOI**
10.3111/13696998.2011.649327

**Original Paper URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adalimumab; Antibodies, Monoclonal, Humanized /administration & dosage /economics /therapeutic use; Anti-rheumatic Agents /administration & dosage /economics /therapeutic use; Arthritis, Rheumatoid /drug therapy /mortality /physiopathology; Cost-Benefit Analysis /methods; Drug Substitution /economics; Etanercept; Female; Finland /epidemiology; Health Resources /utilization; Humans; Immunoglobulin G /administration & dosage /economics /therapeutic use; Male; Outcome Assessment (Health Care); Quality of Life; Receptors, Tumor Necrosis Factor /administration & dosage /therapeutic use; Severity of Illness Index; Treatment Failure

**AccessionNumber**
22012012169

**Date bibliographic record published**
28/05/2012

**Date abstract record published**
18/12/2012