Treatment of follicular non-Hodgkin's lymphoma with or without rituximab: cost-effectiveness and value of information based on a 5-year follow-up

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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 as an induction therapy or as both induction and maintenance therapy, as an addition to treatment for follicular non-Hodgkin’s lymphoma. The authors concluded that the addition of rituximab induction and maintenance could be cost-effective. The methods were satisfactory, but some were poorly reported. The results were well reported. The authors’ conclusions appear to be appropriate, depending on the quality of the trial that provided the effectiveness and some of the resource use data.

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

Study objective
The objective was to evaluate the cost-effectiveness of rituximab as an induction therapy or as both an induction and maintenance therapy as an addition to treatment for follicular non-Hodgkin's lymphoma.

Interventions
Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) was compared with rituximab induction then CHOP, and rituximab induction then CHOP with rituximab maintenance.

Location/setting
Finland/secondary care.

Methods
Analytical approach:
A state-transition Markov model was constructed to determine the costs and benefits of the treatment strategies, using data from a clinical trial of rituximab for follicular non-Hodgkin’s lymphoma. A lifetime horizon was adopted and the authors stated that the perspective was that of the health care provider.

Effectiveness data:
The effectiveness data came primarily from a five-year follow-up of the EORTC20981 trial of rituximab. The main clinical effectiveness estimate was patient survival.

Monetary benefit and utility valuations:
The utility estimates were from a British study of 222 patients with follicular non-Hodgkin's lymphoma. The utilities were estimated using the European Quality of life (EQ-5D) questionnaire for each health state in the model.

Measure of benefit:
The benefit measure was the number of quality-adjusted life-years (QALYs), which were discounted at an annual rate of 3%. Secondary measures were life-years gained and progression-free years.

Cost data:
The analysis included the direct medical costs of the treatment strategies (CHOP and rituximab), the health care resources used (out-patient visits), and the treatment of serious adverse events and relapses. The drug use and adverse event data were from the EORTC20981 trial. The costs of treatment were based on Finnish market prices for
pharmaceuticals, and the costs of health care were based on case-mix adjusted Finnish national unit costs. The costs of serious adverse events were from the diagnosis-related group classification system. All costs were presented in 2008 Euros (EUR) and discounted at an annual rate of 3%.

Analysis of uncertainty:
A univariate sensitivity analysis was performed, varying a number of key model inputs. A probabilistic sensitivity analysis was undertaken, using 2,000 Monte Carlo simulations, and the results were used to generate a cost-effectiveness acceptability frontier (CEAF) and the expected value of perfect information (EVPI).

Results
The expected lifetime cost was EUR 49,562 for CHOP, EUR 59,521 for rituximab induction and CHOP, and EUR 68,331 for rituximab induction and maintenance and CHOP; the addition of rituximab as induction resulted in an additional cost of EUR 8,810, and as induction and maintenance it added EUR 18,769.

The average QALYs were 3.90 with CHOP, 4.72 with rituximab induction, and 5.21 with rituximab induction and maintenance; the addition of rituximab maintenance resulted in a gain of 0.49 QALYs compared with rituximab induction, and 1.31 QALYs compared with CHOP.

Compared with CHOP alone, the incremental cost-effectiveness ratio for rituximab induction and maintenance was EUR 14,360 per QALY gained and for rituximab induction it was EUR 12,123 per QALY gained. Compared with rituximab induction, the incremental cost-effectiveness ratio of induction and maintenance was EUR 18,147 per QALY gained.

The one-way sensitivity analysis found that the results were relatively insensitive to the changes in the key parameters. The CEAF showed that rituximab induction and maintenance was cost-effective in 61.6% of simulations at a EUR 20,000 threshold, 95.3% at a EUR 30,000 threshold, 99.7% at a EUR 40,000 threshold, and 100% at a EUR 50,000 threshold. The EVPI was estimated to be EUR 1,240 at a willingness to pay of EUR 12,123, and EUR 5,196 at a willingness to pay of EUR 18,147 per QALY gained.

Authors' conclusions
The authors concluded that rituximab induction and maintenance could be a cost-effective addition to treatment for Finnish patients with follicular non-Hodgkin's lymphoma.

CRD commentary
Interventions:
The interventions were well described and the analysis included Finnish recommended usual practice for the treatment of patients with relapsed or refractory follicular non-Hodgkin's lymphoma.

Effectiveness/benefits:
The effectiveness data came from one study, which was a long-term follow-up of a trial of rituximab in patients with follicular non-Hodgkin's lymphoma. This trial follow-up was not described making it unclear if it was well designed, if the sample was large enough to produce significant results, and if any confounding analysis was undertaken to address differences between the intervention groups. The authors did state that the design was consistent with Finnish recommendations and practice and they provided references, which should be consulted to assess the quality of the data. The measure of benefit appears to have been appropriate and the source for the utility estimates was described. The patients in this utility study were not Finnish, but the authors stated that no Finnish data were available. It was unclear how this study was chosen, and if the best available evidence was used. The measure of benefit was appropriately discounted.

Costs:
The authors reported the perspective and appear to have included the main costs relevant to this perspective. The sources for the resource estimates were clearly stated and the unit costs were clearly presented. Some of the resource estimates were from the EORTC20981 trial, and as its quality was unclear, their quality is also unclear. The other sources were publicly available and appear to have been appropriate. The authors appropriately discounted the costs and
adjusted for inflation.

Analysis and results:
The analytic approach appears to have been appropriate and the results were reported clearly and in full. Appropriate one-way sensitivity analyses were performed as well as a probabilistic sensitivity analysis, which thoroughly captured the parameter uncertainty. The authors acknowledged and highlighted some limitations of their study. They conducted a systematic review to identify similar Finnish studies and appropriately compared their results with those of these other studies.

Concluding remarks:
The methods were satisfactory, but some were poorly reported. The results were well reported. The authors’ conclusions appear to be appropriate, depending on the quality of the trial that provided the effectiveness data and some of the resource use data.

Funding
Funded by Roche Oy, Finland.

Bibliographic details

PubMedID
21135053

DOI
10.1093/annonc/mdq582

Original Paper URL
http://annonc.oxfordjournals.org/content/22/5/1189.abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Antibodies, Monoclonal, Murine-Derived /economics /therapeutic use; Antineoplastic Combined Chemotherapy Protocols /therapeutic use; Cost-Benefit Analysis; Cyclophosphamide /therapeutic use; Disease-Free Survival; Doxorubicin /therapeutic use; Follow-Up Studies; Health Care Costs; Humans; Kaplan-Meier Estimate; Lymphoma, Follicular /drug therapy /mortality; Markov Chains; Prednisone /therapeutic use; Quality of Life; Recurrence; Rituximab; Treatment Outcome; Vincristine /therapeutic use

AccessionNumber
22011000910

Date bibliographic record published
17/08/2011

Date abstract record published
14/09/2011