Short-course adjuvant trastuzumab therapy in early stage breast cancer in Finland: cost-effectiveness and value of information analysis based on the 5-year follow-up results of the FinHer Trial

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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 examined the cost-effectiveness of trastuzumab as an additional treatment for women with early stage breast cancer, compared with standard care, using the follow-up results of the Finland Herceptin (FinHer) Trial. The authors concluded that nine weeks of trastuzumab treatment was likely to be cost-effective, in Finland, and research should focus on the long-term treatment effect. The methods were valid and should ensure that the authors' conclusions are robust.

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

Study objective
This study examined the cost-effectiveness of trastuzumab as an adjuvant treatment for women with early stage breast cancer, compared with standard care, using the follow-up results from the Finland Herceptin (FinHer) Trial (Joensuu, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details).

Interventions
The intervention was nine weeks of additional trastuzumab treatment, and this was compared with treatment without trastuzumab that consisted of various chemotherapy agents. The nine-week trastuzumab protocol started with a loading dose of 4mg per kg and continued with a weekly dose of 2mg per kg. Upon disease progression, for both groups, patients received trastuzumab in three-week cycles for a maximum of 52 weeks.

Location/setting
Finland/hospital.

Methods
Analytical approach:
The analysis was based a Markov model that simulated the costs and benefits for five years (corresponding to the length of the FinHer Trial) and over the lifetime of the patients. The authors stated that the perspective was societal, excluding the indirect costs, such as productivity losses.

Effectiveness data:
The five-year results of the FinHer Trial provided most of the clinical data, including the transition probabilities and the baseline characteristics of the patient population. Additional inputs were from official Finnish statistics and a published clinical trial of trastuzumab treatment for patients with human epidermal growth factor receptor 2 (HER2) positive metastatic breast cancer. A key assumption was the cessation of the trastuzumab effect beyond the first five years of the simulation, making the two treatment arms equally effective after five years. The key clinical input was the treatment effect, measured by the reduction in disease progression and mortality.

Monetary benefit and utility valuations:
The utility values were from a Swedish study of 361 patients with breast cancer, who completed the European Quality of life (EQ-5D) questionnaire.
Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures and they were discounted at a rate of 3% per annum.

Cost data:
The economic analysis included the costs of hospital treatment for localised or disseminated breast cancer, including trastuzumab, and patient co-payments. The treatment costs were from a Finnish university hospital. The drug costs included acquisition, administration, and preparation. The costs of HER2 testing and cardiac toxicity were excluded as they were the same for both options. All costs were in Euros (EUR) and were discounted at an annual rate of 3%. The price year was 2008.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken by assigning probability distributions to the model inputs. The types of distributions were clearly stated. Cost-effectiveness acceptability curves were generated. One-way sensitivity analyses were carried out on single inputs and alternative scenarios were considered. The expected values of partial and perfect information were calculated to highlight the importance of additional research for some model parameters.

Results
Trastuzumab led to a gain of 0.66 QALYs, 0.85 life-years, and an additional cost of EUR 7,900, over usual care. The incremental cost per QALY gained was EUR 12,000 and per life-year gained was EUR 9,300.

The probability of trastuzumab being cost-effective at a threshold of EUR 30,000 per QALY was 87%. The one-way sensitivity analysis showed that treatment effect was a key input for the model and varying this value, within the 95% confidence interval from the trial data, changed the incremental cost per QALY for trastuzumab from EUR 2,500 to being dominated as it was more expensive and less effective. This was the most uncertain parameter.

The value of information analysis showed that the patient-level expected value of perfect information was EUR 870 at a willingness to pay of EUR 30,000 per QALY.

Authors' conclusions
The authors concluded that the nine-week trastuzumab treatment was likely to be cost-effective, in Finland, and research should focus on the long-term treatment effect.

CRD commentary
Interventions:
The selection of the comparators was appropriate and standard chemotherapy without trastuzumab was the main comparator. A description of the standard chemotherapy would have been useful.

Effectiveness/benefits:
The clinical analysis was based mainly on evidence from one source, which appears to have been appropriate and consistent with the objective that was to use this new evidence on trastuzumab. The methods of the FinHer Trial were not reported, as they had been published elsewhere, but its randomisation should have ensured that the clinical inputs were robust. This study used data with a longer follow-up (five years) than previous economic evaluations, which was an improvement. Appropriate statistical techniques were applied to extrapolate the short-term data to the patients’ lifetimes. The other clinical sources were representative of Finland. The utility values were appropriately from a published study that used a validated instrument for cancer patients. QALYs and life-years were valid measures, as they capture the impact of the disease on both survival and quality of life, which are relevant dimensions of health for breast cancer patients.

Costs:
The authors stated that the analysis was conducted from the societal viewpoint, excluding productivity losses, and the categories of costs reflected this perspective. In general, the unit costs were not presented separately from the resource use reducing the ability to replicate the analysis. Most of the cost data were from a Finnish hospital, which should have been appropriate for the context. Some cost items were excluded as they were common to both treatment arms. Other
details, such as the price year and discount rate, were reported. The cost data were varied in the sensitivity analysis.

Analysis and results:
An incremental approach was appropriately used to synthesise the costs and benefits of the alternative strategies. Both the incremental and the total outputs were presented. Validated approaches were used to investigate the uncertainty and the findings were clearly reported and discussed. The expected value of perfect information was calculated and showed the high uncertainty in some of the model parameters and the importance of further research. The authors compared their results with those from other published studies and pointed out the importance of follow-up in determining the cost-effectiveness of trastuzumab. The results might be transferable to settings with a similar cost structure.

Concluding remarks:
The methods were valid and should ensure that the authors’ conclusions are robust.

Funding
Supported by grants from the Yrjo Jansson Foundation, and the Pharma Industry Finland Research Trust.

Bibliographic details

PubMedID
21299447

DOI
10.3109/0284186X.2011.553841

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Antibodies, Monoclonal /administration & dosage /adverse effects /economics; Antibodies, Monoclonal, Humanized; Antineoplastic Agents /administration & dosage /adverse effects /economics; Breast Neoplasms /drug therapy /economics /pathology; Carcinoma /drug therapy /economics /pathology; Chemotherapy, Adjuvant /economics /methods; Clinical Trials as Topic /statistics & numerical data; Cost-Benefit Analysis; Data Interpretation, Statistical; Drug Administration Schedule; Female; Finland; Follow-Up Studies; Humans; Information Storage and Retrieval /standards; Neoplasm Staging; Predictive Value of Tests; Time Factors; Trastuzumab

AccessionNumber
22011000686

Date bibliographic record published
06/07/2011

Date abstract record published
13/07/2011