Trastuzumab treatment of early stage breast cancer is cost-effective from the perspective of the Belgian health care authorities
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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 assessed the cost-effectiveness of trastuzumab, as an adjuvant therapy, for women with early-stage, human epidermal growth factor receptor 2-positive, breast cancer. The authors recommended that adjuvant trastuzumab was cost-effective for the Belgian health care system. There were some limitations with the sensitivity analysis, but the other study methods were appropriate and comprehensive. The conclusions reached by the authors appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost-effectiveness of trastuzumab, as an adjuvant therapy, for women with early-stage, human epidermal growth factor receptor 2 (HER2)-positive breast cancer.

Interventions
Treatment with trastuzumab was compared with treatment without trastuzumab. Trastuzumab was administered at a loading dose of 8mg per kg on day one, followed by 6mg per kg every three weeks for one year.

Location/setting
Belgium/out-patient care.

Methods
Analytical approach:
An existing Markov model was used to synthesise the published data from various sources, including a key randomised controlled trial. The existing model was adapted to estimate the cost-effectiveness for women at five age ranges. Two hypothetical cohorts of 1,000 patients were modelled over a life-time and the authors stated that the perspective was that of the Belgian health care payer.

Effectiveness data:
The main clinical effectiveness data were the reductions in the risks of local recurrence, metastases during disease-free survival, and metastases during local recurrence. These data were primarily from a one-year follow-up trial and it was assumed that the relative risks from this trial were constant for 10 years and then were relatively increased by 30%. The key adverse events, which were acute and chronic cardiac events, were included and their rates were from published literature. The transition probabilities between health states were based on the extrapolation of data from three published studies.

Monetary benefit and utility valuations:
The health-state values were derived from those published in the literature for the following states; disease-free survival, recurrence, metastatic disease, chronic cardiac event, and death.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and discounting was applied at an annual rate of 1.5%.

Cost data:
The direct medical costs were included for trastuzumab and its administration, heart monitoring, the HER2 test (fluorescence in situ hybridisation), and treatment of cardiac events, disease-free survival, recurrence, and disease metastasis. Patient-level data were obtained for resource use by refined diagnosis-related group code and severity. The opinions of six experts were used for doctor visits, laboratory tests, imaging tests, hospital admissions, and medications during follow-up care. The unit costs were from national sources and they were in Euros (EUR), adapted to the 2005 price year, and discounted at 3% per annum.

Analysis of uncertainty:
The uncertainty was measured in a probabilistic sensitivity analysis, with 800 Monte Carlo simulations (representing Belgian trastuzumab-eligible patients with breast cancer), and 95% confidence intervals were generated. The results were presented in a scatter plot on the cost-effectiveness plane.

Results
With trastuzumab compared against without, the incremental discounted costs ranged from EUR 29,999 for women aged 60 to 69 years to EUR 34,699 for women aged over 80 years. The discounted incremental gain in QALYs ranged from 4.733 for women under 50 years old to 0.361 QALYs for women over 80 years old.

Over the lifetime horizon, the incremental cost per QALY gained ranged from EUR 6,520 for women under 50 years old to EUR 96,150 for women over 80 years old.

Varying the model parameters, in the probabilistic sensitivity analyses, showed that the mean incremental cost per QALY, for all patients, was EUR 10,163. Trastuzumab was cost-effective for women up to 80 years old; for 60- to 69-year-olds the mean was EUR 11,868 per QALY gained. For women over 80 years old, it exceeded the EUR 40,000 willingness-to-pay threshold.

Authors' conclusions
The authors recommended that adjuvant treatment with trastuzumab, for women with HER2-positive early-stage breast cancer, was cost-effective for the Belgian health care system.

CRD commentary
Interventions:
The interventions were adequately described, including the dosage and the average patient weight. Trastuzumab might be an appropriate option in other settings.

Effectiveness/benefits:
The efficacy and health state transition probabilities were from the available published research, including a randomised controlled trial. It was unclear if a systematic review of the literature was undertaken and if all the best available evidence was used. The utility values appear to have been extracted directly from reports of other patients with breast cancer and it is difficult to ascertain the quality of these estimates. The benefit measure was appropriately discounted.

Costs:
The broad cost categories appear to have been relevant to the Belgian health care system perspective and they included cardiac adverse events. The sources for the cost estimates were relevant to the study population and were fully referenced. Future costs were discounted appropriately and details of the price year and currency were provided.

Analysis and results:
The model used to synthesise the evidence appears to have been appropriate and the results were clearly reported. More Monte Carlo simulations (800 patients) compared with the hypothetical cohorts (1,000 each), might have increased the confidence in the findings. The authors reported a number of limitations to their study including the need for assumptions due to a lack of data on the sustainability of the trastuzumab effects over time, the best treatment duration for trastuzumab, and the uncertainty around the adverse event of brain tumours.

Concluding remarks:
There were some limitations with the sensitivity analysis, but the other study methods were appropriate and comprehensive. The conclusions reached by the authors appear to be appropriate.

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