Cost-effectiveness analysis of lapatinib in HER-2-positive advanced breast cancer

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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
The aim was to determine whether the addition of lapatinib to capecitabine was cost-effective compared with capecitabine monotherapy for the treatment of human epidermal growth factor receptor-2-positive breast cancer. The authors concluded that, compared with accepted willingness-to-pay thresholds, the addition of lapatinib to capecitabine was clearly not cost-effective compared with capecitabine monotherapy. The reporting and methods were adequate and the authors’ conclusions appear consistent with the evidence presented.

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

Study objective
The objective was to determine whether addition of lapatinib to capecitabine was cost-effective compared with capecitabine monotherapy for treatment of human epidermal growth factor receptor-2 (HER-2)-positive breast cancer.

Interventions
Capecitabine (2g/m² of body surface area in two doses on days one to 14 of a 21-day cycle) plus lapatinib (1.25g daily) was compared with capecitabine (2.5g/m² of body surface area in two doses on days one to 14 of a 21-day cycle) monotherapy.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The authors used a state-transition Markov model to determine the lifetime clinical and economic impact of the alternative strategies. Data was from a randomised controlled trial (Geyer, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). A lifetime horizon was adopted. The authors stated that the perspective of the study was societal.

Effectiveness data:
Clinical data came from a published randomised controlled trial (Geyer, et al. 2006) and a conference abstract that provided updated efficacy data from the same trial (Geyer, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details) and an open-label single-arm phase II trial (GlaxoSmithKline. 2009, see ‘Other Publications of Related Interest’ below for bibliographic details). The key clinical parameter was time to progression (time from randomisation to disease progression or death). Secondary parameters were overall response rate, progression-free survival and overall survival.

Monetary benefit and utility valuations:
Utility estimates were derived from a number of studies of metastatic breast cancer.

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

Cost data:
The analysis included direct costs related to treatment of HER-2-positive breast cancer (which included drug costs and monitoring, treatment of cardiac events and costs of management of side effects such as severe diarrhoea) and indirect costs (patient time and travel). The costs were derived from a number of published data sources; these included technology appraisals, Medicare reimbursement codes and United States Bureau of Labor Statistics. Costs were expressed in 2007 US dollars ($). A 3% annual discount rate was applied.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were performed to assess the impact of parameter uncertainty on the results. Parameter estimates were varied across a broad range.

Results
Addition of lapatinib to capecitabine (combination therapy) was associated with an increase in survival of 1.96 months compared with capecitabine monotherapy (17.41 months versus 15.45 months). The gain in QALYs was 0.12.

The average total cost of combination therapy per patient was $66,499 compared with $46,869 for monotherapy (an additional cost of $19,630).

The incremental cost-effectiveness ratio of combination therapy was $166,113 per QALY gained ($13,483 per QALM gained).

Probabilistic sensitivity analysis showed that the 95% confidence interval for the incremental cost-effectiveness ratio (ICER) was $158,000 to $215,000 per QALY gained. The probability that the ICER was lower than $100,000 was 1%.

Authors’ conclusions
The authors concluded that compared with accepted willingness-to-pay thresholds, adding lapatinib to capecitabine monotherapy was not cost-effective.

CRD commentary
Interventions:
The interventions were well described. Analysis included an appropriate comparator.

Effectiveness/benefits:
Clinical data came from a range of sources with varying methodological strength. The trials were not described and it was unclear whether they presented direct or indirect evidence for the progression outcomes for the comparators in this analysis. The key clinical inputs were provided in a table. The method for use and extraction of data was described. Little information was provided on the approach to determining the utility estimates and so the methodology used to calculate QALMs was unclear. QALMs were the appropriate measure of benefit due to disease impact on both quality of life and survival.

Costs:
The perspective was clearly defined and it appeared that relevant costs were included, but costs to carers and family were not included as indirect costs. A breakdown of cost items was provided in a table, which enhanced the ability to replicate results for other settings. The price year, sources of data and use of discounting were provided.

Analysis and results:
Use of an incremental analysis was appropriate to determination of relative cost-effectiveness of the alternative regimes. The issue of uncertainty was appropriately addressed with one-way and probabilistic sensitivity analyses. The results of the base-case and sensitivity analyses were well reported, which enhanced the generalisability of the results for other settings. The authors highlighted major assumptions and strengths and limitations of the study.

Concluding remarks:
On the whole, this cost-effectiveness analysis was performed satisfactorily in terms of data selection, methodology and reporting of results. The authors’ conclusions appear appropriate and consistent with the evidence.
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