A cost-effectiveness analysis of adjuvant trastuzumab regimens in early HER2/neu-positive breast cancer


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 adjuvant trastuzumab (AT) therapy, with or without anthracyclines, for early-stage HER2/neu-positive, metastatic breast cancer. It compared three strategies: conventional chemotherapy without trastuzumab, anthracycline-based AT and non-anthracycline based AT. The study demonstrated the cost-effectiveness of either AT option, although assumptions about the long-term effectiveness of treatment heavily affected the authors’ conclusions.

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

Study objective
The objective of the study was to assess the cost-effectiveness of adjuvant trastuzumab (AT) therapy, with or without anthracyclines, for early-stage HER2/neu-positive, metastatic breast cancer in a hypothetical cohort of 49-year-old women.

Interventions
Three health interventions were considered: conventional chemotherapy without trastuzumab (NT), anthracycline-based AT (A-AT) and non-anthracycline AT (nonA-AT). NT consisted of doxorubicin 60 mg/m$^2$ plus cyclophosphamide 600 mg/m$^2$ intravenously for 4 cycles every 3 weeks, followed by paclitaxel 80 mg/m$^2$ intravenously for 12 cycles every week. A-AT consisted of the same chemotherapy of NT, with the addition of trastuzumab administered weekly concurrently with paclitaxel (initial dose 4 mg/kg, then doses of 2 mg/kg up to 1 year). NonA-AT consisted of docetaxel 75 mg/m$^2$ plus carboplatin, with trastuzumab added at the same dose as for A-AT.

Location/setting
USA/hospital.

Methods
Analytical approach:
This economic evaluation was based on a Markov model, which was constructed to simulate the management of patients eligible for adjuvant treatment. A patient’s lifetime horizon was considered. The authors stated that a societal perspective was adopted.

Effectiveness data:
Short-term data on breast cancer recurrence rates for the three treatments compared were based on the pooled results from two clinical trials: the National Survival Adjuvant Breast and Bowel Project (NSABP) B-31 and the North Central Cancer Treatment Group (NCCTG) N9831 trials. The assumptions used to extrapolate treatment effectiveness to longer follow-up periods were based on published data on survival after HER2/neu-amplified BC. Non-cancer mortality data were derived from the National Center for Vital Statistics.

Monetary benefit and utility valuations:
The utility estimates were derived from published studies, one of which used time trade-off assessments.

Measure of benefit:
The summary benefit measure was the quality-adjusted life-years (QALYs). These were estimated using the decision model. Life-years (LYs) were also calculated in an alternative analysis. The benefits were discounted at an annual rate of 3%.

Cost data:
The health services included in the analysis were drugs (acquisition and administration), oncologist visits, cardiac monitoring, supporting care and time lost from work because of treatment. The costs and resources used came from published sources, including publications linked with the Cancer Surveillance System of the US Surveillance, Epidemiology, and End Results database. Drug dosages were based on the two pivotal clinical trials used for clinical estimates (NSABP and NCCTG). The costs were in 2005 US dollars ($). An annual discount rate of 3% was applied.

Analysis of uncertainty:
Key clinical assumptions on the declining benefits of therapies or the impact of side-effects (i.e. cardiac toxicity) were investigated using a probabilistic sensitivity analysis with 95% confidence intervals from randomised clinical trials (RCTs). All other model inputs were varied in a one-way sensitivity analysis, using published data or +/-20% of the base-case values. An alternative scenario assumed no benefit from AT after 4 years from the beginning of treatment.

Results
The expected total costs were $133,429 with NT, $190,092 with A-AT and $206,561 with nonA-AT. The expected QALYs (LYs) were 9.35 (12.29), 10.77 (14.01) and 10.61 (13.56), respectively.

The incremental analysis showed that nonA-AT was dominated by A-AT, which was simultaneously more effective and less expensive. The incremental cost per QALY gained with A-AT over NT was $39,892 ($32,816 per LY gained).

The results of the probabilistic sensitivity analysis showed that nonA-AT remained a dominated alternative in most scenarios, while incremental cost-effectiveness ratios worsened dramatically when recurrence rates were only minimally improved with either AT strategy.

The deterministic sensitivity analysis suggested that model results were sensitive to variations in the discount rate, cost of AT, survival after breast cancer recurrence, and the cost of treating metastatic breast cancer. However, assumptions about the duration of AT benefits were the key input of the model: assuming no benefit after 4 years from the beginning of treatment led to an incremental cost per QALY of $142,516 for A-AT and of $157,078 compared with NT.

Authors' conclusions
The authors concluded that AT regimens were economically attractive from the perspective of US society for the treatment of early-stage HER2/neu-positive, metastatic BC. However, additional information on the long-term impact of AT would make the cost-effectiveness of these regimens clearer.

CRD commentary
Interventions:
The rationale for the choice of the comparators was clear in that current available therapies were examined. Dosages were based on pivotal clinical trials. They are likely to be valid comparators in other settings.

Effectiveness/benefits:
The clinical estimates appear to have been identified selectively rather than through a systematic review of the literature. However, the pivotal RCTs selected represent a valid source of data, owing to the strengths of this design. Assumptions had to be made about the long-term effect of AT, given the lack of data. The most uncertain inputs of the model were varied in the sensitivity analysis, showing high variability in the study results. The sources used to derive quality-of-life estimates were not described clearly. Nevertheless, the use of QALYs (and LYs) has the advantage of making the benefit measures comparable to those in other studies.

Costs:
The health services included in the analysis were consistent with the perspective adopted. However, the costs were often
presented as macro-categories and little information on the quantities of resources used was provided. This may limit
the possibility of replicating the analysis in other settings. Furthermore, the sources used in the analysis were not
described in depth. The authors pointed out that the costs of ascertaining HER2/neu status were not included. If they
were, the cost-effectiveness of the AT strategies would be less favourable. The influence of key cost items on the study
results was investigated in the sensitivity analysis.

Analysis and results:
The use of an incremental analysis to synthesise the costs and benefits of the alternative strategies was appropriate. In
effect, less cost-effective strategies were excluded by dominance. The results of both the base-case and sensitivity
analyses were presented clearly in the tables and graphics. The issue of uncertainty was satisfactorily addressed,
especially with respect to the most doubtful estimates of treatment effectiveness.

Concluding remarks:
The results of the analysis were presented clearly and most of the sources used to derive the clinical data were
appropriate. Thus, even if more details of the derivation of some model inputs would have been useful, overall, the
authors’ conclusions appear valid.

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Bibliographic details

Other publications of related interest
Wapnir IL, Aebi S, Geyer CE, et al. A randomized clinical trial of adjuvant chemotherapy for radically resected
Baselga J, Perez EA, Pienkowsky T, Bell R. Adjuvant trastuzumab: a milestone in the treatment of HER-2-positive

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