Trastuzumab in adjuvant breast cancer therapy: a model based cost-effectiveness analysis  

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.

Health technology
The study compared two strategies for the treatment of breast cancer. The FEC100 regimen (fluorouracil, epirubicin 100 mg/m2, cyclophosphamide), which was administered for 6 cycles on a 3-weekly basis, was compared with the same regimen followed by 3-weekly administration of trastuzumab for 17 cycles. Trastuzumab was administered at a loading dose of 8 mg/kg after adjuvant chemotherapy and subsequently at a dose of 6 mg/kg at 3-weekly intervals for 1 year (16 courses).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
As this was a modelling study, the population comprised women aged between 20 and 70 years with early breast cancer and who over-express human epidermal growth factor receptor (HER-2). No further inclusion or exclusion criteria were reported.

Setting
The setting was not explicitly stated, but it appears to have been secondary care. The economic study was carried out in the Department of Oncology, University Hospital of North Norway (UNN).

Dates to which data relate
The clinical data were derived from sources published in 2005. The costs and resource use data were derived from official sources and studies published between 2000 and 2006. All costs were reported for the price year 2006.

Source of effectiveness data
The main clinical parameters included:

the rate of breast cancer,
the life expectancy,
the survival rate,
the rate of congestive heart failure due to the addition of trastuzumab, and
death.
Modelling
The authors constructed a decision analytic model to estimate the incremental benefits and costs that arise from the addition of trastuzumab to standard treatment, and to perform a marginal analysis. The time horizon of the model, the health states and modelling assumptions were presented in full.

Sources searched to identify primary studies
The clinical effectiveness data were derived from large international multi-centre randomised trials and a large cohort study that had been published in peer-reviewed journals. The cancer rate was derived from the Norwegian National Cancer Registry. Based on all reports identified, the authors used distant relapse-free survival as a surrogate for future overall survival and employed two absolute improvement rates (10% and 20%) caused by trastuzumab in their analysis.

Methods used to judge relevance and validity, and for extracting data
The authors only included survival data from studies that had been published in peer-reviewed journals. It was reported that a published study that referred to a small sample size and short time horizon of analysis was excluded from the review. No further inclusion criteria for any parameters were specified. The methods used to select the estimates were not reported. The methods used to adjust survival to obtain prolonged survival were reported in full.

Measure of benefits used in the economic analysis
The authors used the life-years gained (LYG) and the quality-adjusted life-years (QALYs) as measures of benefit in the economic analysis. The LYG were obtained from the model, while the quality of life estimate (for the estimation of QALYs) was obtained from published literature.

Direct costs
The analysis accounted for marginal health service costs per patient, incurred by the addition of trastuzumab to standard treatment. These included trastuzumab medication, cardiac check-ups, pharmacy administration, visits to outpatient clinic, congestive heart failure treatment and travel costs. Net savings due to metastatic treatment and subsequent chemotherapy avoided were also accounted for in the analysis. These costs included the cost of drugs and chemotherapy (e.g. docetaxel, trastuzumab, vinorelbine, capecitabine, paclitaxel), all the above-mentioned categories, and the cost of computed tomography scans and X-rays. The costs and the quantities were analysed separately. The costs were derived from the authors' setting (UNN), while resource use was mainly obtained from published sources. The costs of assessing HER-2 were excluded from the analysis as they were assumed to be equal in both groups. The costs were appropriately discounted at an annual rate of 3%. The costs were reported for the price year 2006.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Marginal productivity losses due to the addition of trastuzumab to standard treatment were accounted for, as were productivity gains due to metastatic treatment and chemotherapy forgone due to the addition of trastuzumab to standard treatment. The costs and the quantities were reported separately. Resource use was derived from published sources, while the cost data were obtained from national official sources (Statistics Norway). The costs were appropriately discounted at a rate of 3%. The costs were reported for the price year 2006.

Currency
Norway kroner (NOK). The costs were converted to euros (EUR) at the rate of EUR 1.00 = NOK 8.02 (6 February 2006).
Sensitivity analysis
Parameter uncertainty was investigated through one-way sensitivity analyses. The model parameters investigated were the discount rate, outpatient treatment costs, travel, administration, price of trastuzumab, production gains and LYG. The discount rate was varied between 0 and 5% while all other parameters were varied by +/-25 % around the base-case estimates.

Estimated benefits used in the economic analysis
The addition of trastuzumab to standard treatment improved overall survival by 1.1 LYG when assuming a 10% overall improvement in survival, and by 2.19 LYG when assuming a 20% overall improvement in survival. While discounted results are presented here, the paper also presented the undiscounted results.

Cost results
The total costs per patient treated were EUR 17,844, when savings due to future treatment forgone were included (accounting for future productivity gains, a societal perspective). Other cost results were presented in full.

Synthesis of costs and benefits
Over a 10-year period, the cost per LYG ranged from EUR 8,148 to EUR 30,290 (for 20% and 10% overall improvements in survival, respectively).

The cost per QALY ranged from EUR 10,185 for a 20% overall improvement in survival to EUR 37,862, for a 10% overall improvement in survival.

The costs and benefits were discounted at a rate of 3%.

The sensitivity analyses demonstrated that the results were most sensitive to variations in the LYG, the price of trastuzumab, production gains and the discount rate.

Authors' conclusions
Trastuzumab would appear to be a cost-effective option in adjuvant treatment of human epidermal growth factor receptor (HER-2)-positive breast cancer patients, provided that a minimum of 8% improvement in absolute 10-year overall survival is accomplished.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was explicitly justified. Both regimens appear to have represented officially recommended treatment options in the authors' setting. You should decide if they represent widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
The model parameters were obtained from published literature. However, the authors do not appear to have undertaken a systematic review. The data were obtained solely from primary studies published in peer-reviewed journals, mainly large randomised trials which potentially have a high level of internal validity. However, it is not possible to comment on the validity of the data given the information provided in this paper.

Validity of estimate of measure of benefit
QALYs and LYG were used as measures of benefit in the economic analysis. The estimates were mainly derived from published studies and the method used to derive the utility weights was not discussed.

Validity of estimate of costs
A societal perspective was adopted in the economic analysis. As such, it appears that all the relevant categories of costs have been included. However, potential side-effects of the treatment options were not discussed. The costs for assessing HER2, treatment in a terminal care setting, and the costs of hormonal therapy were excluded because the data were unavailable, although their omission is unlikely to have affected the authors' conclusions. The resource quantities and the costs were reported separately, as were dates for the prices. The costs were treated deterministically, but an extensive sensitivity analysis was performed to assess the robustness of the estimates used. This enhances the generalisability of the results to other settings.

Other issues
The authors compared their findings with those from other studies which, in general, were in agreement. The authors acknowledged variation in productivity costs between settings, and the impact of this on the economic results was evaluated in a sensitivity analysis. The authors do not appear to have presented their results selectively, although the results of the sensitivity analysis were not presented in detail. The authors' conclusions would appear to be an accurate reflection of the scope of their analysis.

The authors presented a number of limitations to their study. For example, overall survival improvement was based on clinical data and might have been higher than that observed in "real life". In addition, the employment of different time horizons in the analysis would have provided a better reflection of "real life". The authors acknowledged that the estimation of QALYs was based on utility values that were not disease- and treatment-specific, and this might introduce uncertainty into the results.

Implications of the study
The authors did not make explicit recommendations for changes in policy or practice. Future research should evaluate the effectiveness of trastuzumab treatment regimens of short duration.

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