Cost effectiveness of TAC versus FAC in adjuvant treatment of node-positive 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
This study examined the cost-effectiveness of docetaxel in combination with doxorubicin and cyclophosphamide compared with 5-fluorouracil in combination with doxorubicin and cyclophosphamide, after primary surgery for women with operable, axillary lymph node-positive breast cancer. Docetaxel offered improved survival, compared with fluorouracil, and it provided good value for money from the perspective of the public payer. The study appears to have been based on a valid cost-effectiveness framework, which should ensure the validity of the authors’ conclusions.

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

Study objective
This study examined the cost-effectiveness of docetaxel in combination with doxorubicin and cyclophosphamide compared with 5-fluorouracil in combination with doxorubicin and cyclophosphamide, after primary surgery for women with operable, axillary lymph node-positive breast cancer.

Interventions
The docetaxel regimen consisted of docetaxel 75mg per m$^2$ infused over one hour, with doxorubicin 50mg per m$^2$ and cyclophosphamide 500mg per m$^2$. The fluorouracil regimen consisted of 5-fluorouracil 500mg per m$^2$, with doxorubicin 50mg per m$^2$ and cyclophosphamide 500mg per m$^2$. All treatments were given as intravenous infusions on day one of a three-week cycle, for six cycles.

Location/setting
Canada/secondary care and hospital.

Methods
Analytical approach:
The analysis was based on a Markov model that considered five years of treatment and the long-term follow-up. The authors stated that the analysis was conducted from the perspective of a Canadian provincial government payer.

Effectiveness data:
The clinical evidence was mainly from a published multicentre phase III randomised controlled trial (RCT), namely the Breast Cancer International Research Group (BCIRG) 001 trial (Martin et al 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). This trial enrolled 1,491 women, aged between 18 and 70 years, with axillary node-positive breast cancer. They were randomised to six cycles of either the docetaxel or the fluorouracil regimen, as additional chemotherapy after surgery. The women were followed-up for five years and data on the treatment effect and adverse events were recorded. Overall survival and disease-free survival were the key outcomes for the clinical analysis.

Monetary benefit and utility valuations:
The utility values were derived from published studies and considered the disutility associated with chemotherapy from the BCIRG trial.

Measure of benefit:
Life-years (LYs) and quality-adjusted life-years (QALYs) were the summary benefit measures, and they were discounted at an annual rate of 5%.
Cost data:
The economic analysis included the costs of drug acquisition (docetaxel and fluorouracil regimens), chemotherapy administration for subsequent lines, relapse and follow-up, management of adverse events (febrile neutropenia, stomatitis, diarrhoea, and infection), and granulocyte-colony stimulating factor (G-CSF) prophylaxis. The costs were from the drug manufacturer, Cancer Care Ontario, and other official tariffs. The resource use data were from practice guidelines, the BCIRG trial, and other published evidence. A breakdown of the main cost categories was provided. The costs were in 2006 Canadian dollars (CAD) and a 5% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analysis and bootstrapping were carried out to assess how robust the base-case results were to variations in the key parameters. In an alternative scenario, G-CSF was given as primary prophylaxis.

Results
The incremental cost per LY gained with the docetaxel over the fluorouracil regimen was CAD 6,921.24 and the incremental cost per QALY gained was CAD 6,848.39. When primary prophylaxis with G-CSF was included, the incremental ratios were just above CAD 13,000.

In general, variations in the model parameters did not alter the cost-effectiveness results. With bootstrapping, the incremental cost per QALY gained was CAD 3,060.59 in the best-case scenario and CAD 20,036.64 in the worst-case scenario.

Authors' conclusions
The authors concluded that the docetaxel regimen offered improved survival compared with the fluorouracil regimen, and provided good value for money from the perspective of the public payer.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the two chemotherapy regimens were relevant for the patients studied. The doses and frequency of administration were provided.

Effectiveness/benefits:
The clinical data were mainly from the BCIRG trial and its multicentre and randomised design should ensure the validity of these data. The long follow-up and the large sample size were good features of the trial, but more details of its methods would have been useful. Little information was presented on the assessment of the utility values for the calculation of the QALYs. The impact of variations in these inputs was considered in the sensitivity analysis. Both benefit measures appear to have been appropriate for capturing the impact of the disease on a patient’s health. LYS and QALYs can also be compared with the benefits of other health care interventions.

Costs:
The categories of costs and their sources were consistent with the perspective of the public payer. Most of the costs were presented as category totals, but the unit costs were reported for some categories. The patterns of treatment reflected conventional guidelines for this patient population and appear to be generalisable to other health care settings. A detailed description of each category of cost was provided and the sensitivity analysis considered variations in most of these categories.

Analysis and results:
The projected costs and benefits were not reported, but they were synthesised using a valid incremental approach. The issue of uncertainty was appropriately investigated, using valid methods, and the findings were clearly reported and discussed. An extensive description of the decision model and its pathways was provided. The authors stated that the clinical data from the BCIRG trial and the assumptions on long-term costs might not represent real-life experience.

Concluding remarks:
The study appears to have been based on a valid cost-effectiveness framework, which should ensure the validity of the authors’ conclusions.
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