Docetaxel in combination with doxorubicin and cyclophosphamide as adjuvant treatment for early node-positive breast cancer: a cost-effectiveness and cost-utility analysis

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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 evaluated the cost-effectiveness of two adjuvant regimes in women with node-positive early breast cancer. Docetaxel, doxorubicin, and cyclophosphamide (TAC) was compared with fluorouracil, doxorubicin, and cyclophosphamide (FAC). The authors concluded that TAC was cost-effective compared with FAC in the UK, as well as TAC with primary granulocyte colony-stimulating factor prophylaxis. Except for a concern about relevant comparators, the methodology was appropriate and clearly and transparently reported. The conclusions reached by the authors reflect the scope of the analysis.

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

Study objective
The aim was to evaluate the cost-effectiveness of two adjuvant chemotherapy regimes for women with node-positive early breast cancer. Docetaxel, doxorubicin, and cyclophosphamide (TAC) was compared with fluorouracil, doxorubicin, and cyclophosphamide (FAC).

Interventions
The regimes comprised the administration of six cycles of TAC or FAC based on the Breast Cancer International Research Group 001 trial (BCIRG 001, Martin, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details).

Location/setting
UK/secondary or tertiary care.

Methods
Analytical approach:
A decision tree and a Markov model with monthly cycles were used to synthesise the data. A time horizon which ranged from 5 to 40 years (10 years for the base-case) was adopted. The reported perspective was that of the UK National Health Service (NHS).

Effectiveness data:
The main clinical parameters (the effect of chemotherapy on toxicity and outcomes) were derived from patient-level data (see Martin, et al. 2005) obtained from a Phase III randomised controlled trial, with a median follow up of 55 months and involving 1,491 patients. No other trial details were provided. The main estimates were for disease-free survival. The individual data was used to estimate the probabilities for the model and it was extrapolated to predict the events beyond the trial.

Monetary benefit and utility valuations:
The utility weights for remission were derived from the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire, the QLQ-C30, from 929 patients from the BCIRG 001 trial, and converted to utilities using a published algorithm. The utilities for health states post-relapse, as well as the utility decrement due to adverse events, were obtained from the literature.
Measure of benefit:
The benefit measures were life-years (LYs) and quality-adjusted life-years (QALYs). A 3.5% discount rate was applied.

Cost data:
The direct costs included drug costs, administration costs, those associated with receiving granulocyte colony-stimulating factor (G-CSF), and those related to adverse events. Additionally, monitoring costs, hospital costs in relapsed patients, and the primary care costs post-relapse were considered. Adjuvant hormone and radiotherapy costs were excluded, as they did not differ between the groups. The resource use data for patients who relapsed were based on an observational data set collected at a UK university hospital. All prices were reported in 2005 UK pounds sterling (£) and in Euros (EUR) using market exchange rates. An annual discount rate of 3.5% was used.

Analysis of uncertainty:
Parameter uncertainty was investigated through the use of probabilistic sensitivity analysis, which was performed using 1,000 samples of the statistical distributions associated with the key model parameters. Additionally, the impact of using different methods for extrapolating the survival beyond the trial period, the impact of giving G-CSF prophylaxis to all TAC patients, subgroups and univariate analyses, and changing the time horizon were tested.

Results
The estimated mean LYs for the TAC cohort were 7.194, and for the FAC cohort were 6.821, an incremental LY gain of 0.374.

The estimated mean QALYs for the TAC cohort were 5.517, and for the FAC cohort were 5.201, an incremental gain of 0.317.

The mean total costs were £15,587 for TAC and £9,828 for FAC, which is an incremental cost of £5,759.

The incremental ratios from the probabilistic analysis were £15,400 (95% confidence interval, CI: £13,734, £17,997) per LY gained and £18,274 (95% CI: £14,161, £32,422) per QALY gained. Deterministic estimates were also presented.

The sensitivity analysis suggested that the most influential parameter was the time horizon: the cost per QALY was £58,201 at five years, and £9,865 for the lifetime analysis. The method used to extrapolate the trial outcomes beyond the available follow-up had an impact on the results, with a cost per QALY ranging from £15,588, when assuming a continuation of the treatment effect beyond the trial follow-up, to £28,782 per QALY, when assuming no continuation of the treatment effect.

The model was also sensitive to the extreme utility weights for patients in remission, and the scenario in which all TAC patients received primary prophylaxis with pegfilgrastim. The subgroup analysis suggested that TAC was more cost-effective in patients who were younger, oestrogen-receptor–negative, and with fewer positive nodes and lower tumour grades.

Authors’ conclusions
The authors concluded that adjuvant TAC was cost-effective compared with FAC in the UK, as well as TAC with primary G-CSF prophylaxis. The short-term disadvantages were small compared with the long-term benefits. The primary uncertainty in the analysis lay in the extrapolation of outcomes beyond the available trial follow-up data.

CRD commentary
Interventions:
The article provided adequate detail about the interventions compared. However, the authors stated that FAC was not commonly used in the UK and that they used this regimen as a proxy for fluorouracil, epirubicin, and cyclophosphamide (FEC). Whilst this claim was supported by references it is not clear why FEC was not included as a comparator.
Effectiveness/benefits:
The study was based on the analysis of data from one large trial, and it was not made clear or discussed whether this was the only comparative evidence for the treatments. The use of one trial, if other relevant evidence was available, could be considered a weakness of the study. The trial was reported in limited detail but appeared to be of good quality, to fully assess the validity the reader would need to refer to the clinical trial paper. The utilities for remission were derived using an appropriate quality of life (QoL) questionnaire which was administered to patients in the BCIRG 001 trial. These data were then converted using a published algorithm. The trial did not obtain post-relapse QoL data and so these utility weights were taken from another published source. Adverse events were considered throughout the model. Overall, the reporting was clear and transparent.

Costs:
All the relevant costs appear to have been considered for the perspective. The exclusion of some common costs prevents the calculation of the total intervention costs, but does allow analysis of the differences in costs between the comparators. The measurement of resource use was based on real world data from a UK hospital, though it was not described in detail this is likely to provide the most accurate estimate of resource consumption. The costing appears to have been conducted using appropriate methods and was well reported.

Analysis and results:
The authors reanalysed patient level data from one trial to derive the main parameters for the model, as well as extracting some other inputs from published sources. The model structure was presented graphically and well reported. Parameter uncertainty was assessed through probabilistic analysis and a number of alternative scenarios. One of the main limitations may be the lack of long term follow-up data, which led to extrapolation of the trial outcomes. This limitation was acknowledged by the authors.

Concluding remarks:
Except for the concern about relevant comparators, the methodology of the study was appropriate and clearly and transparently reported. The conclusions reached by the authors reflect the scope of the analysis.

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Combined Chemotherapy Protocols /administration & dosage /adverse effects /economics /therapeutic use; Axilla; Breast Neoplasms /drug therapy /economics /pathology /surgery; Chemotherapy, Adjuvant; Cost-Benefit Analysis; Cyclophosphamide /administration & dosage /economics; Decision Trees; Disease-Free Survival; Doxorubicin /administration & dosage /economics; Female; Fluorouracil /administration & dosage /economics;