Cost-Utility Model to Evaluate Adjuvant Chemotherapy for Early Breast Cancer in the United States

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BACKGROUND

Several new interventions have recently become available for the adjuvant treatment of early breast cancer (EBC); these treatments are effective in reducing the incidence of disease relapse.

OBJECTIVE

To develop a model to evaluate the cost-effectiveness and cost-utility of new EBC interventions in the United States (US)

METHODS

- A previously published model[1] was adapted for the US. The time horizon of the analysis was varied from 5 years to 40 years; costs were expressed in US dollars for the cost year 2008. Costs and outcomes were discounted at 3.0% per annum.
- Two interventions were compared for the adjuvant treatment of node-positive EBC patients:
  - TAC = docetaxel (75 mg/m^2), doxorubicin (50 mg/m^2), and cyclophosphamide (500 mg/m^2) (6 cycles)
  - FAC = fluorouracil (500 mg/m^2), doxorubicin (50 mg/m^2), and cyclophosphamide (500 mg/m^2) (6 cycles)
- A combined decision tree and Markov model estimated costs and outcomes from initiation of adjuvant chemotherapy to death (Figure 1). A cohort of 1,000 women with node-positive EBC (median age of 49 years, 55% premenopausal, 76% estrogen or progesterone receptor positive), who were disease free after locoregional surgery, were entered into the Markov model. Patients remained in the remission health state unless they had a relapse (locoregional or distant) or died as a result of other causes.
- The analysis of events postrelapse was simplified to a series of three payoffs: the total expected survival, quality-adjusted life-years (QALYs), and cost postrelapse. These payoffs represented the average experience of relapsing patients, including those achieving long-term remission after first locoregional recurrence and those developing further locoregional and/or metastatic disease. The decision tree component was used to estimate the costs of adjuvant chemotherapy and the impact of adverse events (AEs) on costs and health-related quality of life (HRQoL), with and without primary granulocyte colony-stimulating factor (G-CSF) prophylaxis.
- Parametric survival functions were fitted to patient-level data from trial BCIRG 001,[2] and time-dependent transition probabilities for disease relapse were estimated.[1] Survival postrelapse was estimated from trial BCIRG 001; the proportion of time spent in each health state postrelapse was estimated from an observational dataset of 571 women treated between 1992 and 2004 at the Western General Hospital in Edinburgh, United Kingdom, of whom 180 had a relapse.
- Grade 3/4 or severe to life-threatening events that occurred in more than 1% of patients in either trial arm and at a difference of greater than 2% between arms were included (anemia, asthenia, diarrhea, febrile neutropenia, pain, stomatitis, and vomiting). Probabilities were derived from trial BCIRG 001.
- Costs were estimated from US databases (Pharmetrics medical and prescriptions claims database and Premier hospital database) and a published retrospective analysis of linked Surveillance, Epidemiology and End Results (SEER) Medicare data for 1,580 EBC patients with disease recurrence (cost year = 2008). Drug costs assumed an average body surface area of 1.81m^2, an average weight of 74.7 kg,[3] and that unused drug in opened vials is discarded. The number of cycles was estimated by treatment group from drug use in trial BCIRG 001.
- Utility weights were estimated from European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 data collected in trial BCIRG 001 using a published algorithm,[4] and published literature.[5,6,7,8]
- Probabilistic sensitivity analysis was performed and included the following key parameters: probability of relapse, mean survival postrelapse, time in individual health states postrelapse, mean number of chemotherapy cycles, probabilities of AEs, cost postrelapse, costs of AEs, and utility weights.
- An automated univariate sensitivity analysis was performed (varying all parameters by ± 50% of base-case values). Alternative scenarios were programmed to explore uncertainty beyond the trial follow-up period.

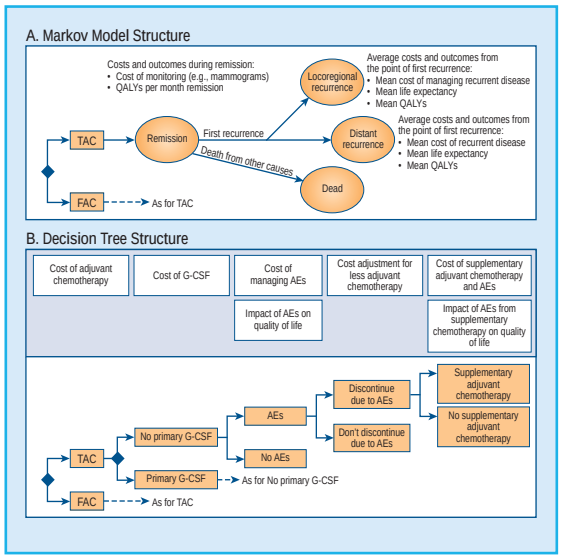

Figure 1. Schematic Representation of the Model Structure

RESULTS

- Mean total expected lifetime costs and outcomes were significantly higher for the TAC cohort. Incremental costs were $19,732 (95% confidence interval [CI]: $15,869-$31,441); life-years gained were 0.93 (95% CI: 0.87-0.97), and QALYs gained were 0.74 (95% CI: 0.44-0.91) (Table 1).
- Incremental cost-effectiveness ratios for TAC versus FAC were $21,318 per life-year saved (95% CI: $16,953-$33,856) and $26,654 per QALY gained (95% CI: $18,553-$50,554).
- In the probabililistic sensitivity analysis, 100% of simulations fell below a threshold of $50,000 per life-year saved (Figure 2).
- Using several alternative methods of estimating the long-term risk of relapse, the incremental cost per life-year saved varied from $12,735 to $30,117.
- In univariate sensitivity analysis, results were most sensitive to the utility weight for remission postchemotherapy. The incremental cost per life-year saved remained below $50,000 for all parameter estimates.

	TAC	FAC	Incremental (TAC–FAC)
Mean cost per patient (95% CI)	$33,379 ($27,530-$48,320)	$13,647 ($10,764-$17,707)	$19,732 ($15,869-$31,441)
Mean life-years per patient (95% CI)	12.43 (12.04-12.94)	11.51 (11.08-12.05)	0.93 (0.87-0.97)
Mean QALYs per patient (95% CI)	9.53 (6.18-11.54)	8.79 (5.72-10.64)	0.74 (0.44-0.91)

Table 1. Base-Case Results

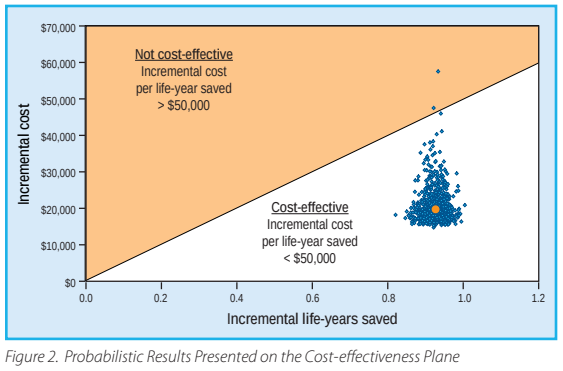

Figure 2. Probabilistic Results Presented on the Cost-effectiveness Plane

DISCUSSION

- The primary uncertainty in the analysis is the extrapolation of outcomes beyond the available trial follow-up.
- The base-case analysis assumes the same risk of relapse in both FAC and TAC cohorts after trial end. The 2005 Oxford overview[9] suggests that disease-free survival curves for alternative adjuvant regimens continue to diverge until at least 10 years postrandom assignment. Thus it is likely that this analysis provides a conservative estimate of the long-term benefit of TAC.
- Using several alternative methods of estimating the long-term risk of relapse, the incremental cost per QALY varied from $12,735 to $30,117. Thus, the considerable uncertainty inherent in the extrapolation is unlikely to alter the cost-effectiveness of TAC over FAC.
- In univariate sensitivity analysis, in which all model parameters were investigated, the incremental cost per life-year saved remained below $50,000 for all parameter estimates.

CONCLUSION

- The model provides a robust framework for estimating cost-effectiveness, allowing exploration of critical areas of uncertainty.
- Use of adjuvant TAC rather than FAC for node-positive early breast cancer patients is cost-effective in the US setting, despite the increased drug cost and the cost and quality-of-life implications of toxicity.

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REFERENCES

1. Wolowacz SE, Cameron D, Tate H, Bagust A. Docetaxel in combination with doxorubicin and cyclophophamide (TAC) as adjuvant treatment for early node-positive breast cancer: a cost-effectiveness and cost-utility analysis. J Clin Oncol 2008;26:925-33.
2. Martin M, Pienkowski T, Mackey J, Pawlicki M, Guastalla JP, Weaver C, et al. Adjuvant docetaxel for node-positive breast cancer. N Engl J Med 2005;352:2302-13.
3. Ogden CL, Fryar CD, Carroll MD, Flegal KM. Mean bodyweight, height, and body mass index, United States 1960–2002. Advance data from vital and health statistics; no 347. Hyattsville, Maryland: National Center for Health Statistics; 2004.
4. Kind P. Measuring the value of quality of life in cancer: an index based on EORTC QLQ-C30. Presented at the 41st Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida. May 13-17, 2005.
5. Hillner BE, Smith TJ. Efficacy and cost-effectiveness of adjuvant chemotherapy in women with node-negative breast cancer. N Engl J Med 1991;324:160-8.
6. Ossa D, Briggs A, Cowell W, Littlewood T, Sculpher M. Utility associated with severity of cancer-related anaemia (CRA): a societal valuation. Presented at the 7th Annual European Congress of the International Society for Pharmacoeconomics and Outcomes Research, Hamburg, Germany. October 24-26, 2004.
7. Launois R, Reboul-Marty J, Henry B, Bonneterre J. A cost-utility analysis of second-line chemotherapy in metastatic breast cancer: docetaxel versus paclitaxel versus vinorelbine. Pharmacoeconomics 1996;10:504-21.
8. Brown R, Hutton J. Cost-utility model comparing docetaxel and paclitaxel in advanced breast cancer patients. Anticancer Drugs 1998;9:899-907.
9. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687-717.

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