Cost-effectiveness of switching to exemestane after 2 to 3 years of therapy with tamoxifen in postmenopausal women with early-stage 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
The study assessed the cost-effectiveness of switching to exemestane after 2 or 3 years' tamoxifen therapy, compared with the current strategy of continuing on tamoxifen, in postmenopausal women with early-stage breast cancer. The authors concluded that exemestane was a cost-effective strategy in the US setting, especially in women with hormone receptor-positive cancer. The quality of the study methodology was good and the authors’ conclusions are robust.

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

Study objective
The primary objective of the study was to assess the cost-effectiveness of switching to exemestane, an aromatase inhibitor used for therapy in postmenopausal women with early-stage breast cancer (BC), after 2 or 3 years of tamoxifen therapy in comparison with the current strategy of continuing on tamoxifen over 5 years.

Interventions
The two adjuvant therapies under examination were switching to exemestane after 2 or 3 years of tamoxifen therapy versus continuing on tamoxifen for 5 years. These therapies were administered to postmenopausal women with early-stage BC. Both hormone receptor (HR)-positive and HR-unknown women were considered.

Location/setting
USA. Secondary care/hospital.

Methods
Analytical approach:
This economic evaluation was based on a Markov model that was developed to predict the long-term clinical and economic impact of the two strategies. The time horizon of the analysis was 35 years (patients’ lifetime since women were assumed to have an average age of 64 years at model entry). The perspective adopted in the study was not explicitly stated.

Effectiveness data:
The clinical estimates used to populate the decision model were identified through a selection of recent and relevant studies. However, the authors did not report details of a review of the literature. Disease- and treatment-related events (mainly osteoporosis for exemestane) were derived from the exemestane pivotal trial (Intergroup Exemestane Study, IES), which followed patients for a maximum of 48 months. A second key source of data was the Surveillance Epidemiology and End Results (SEER) database, covering 12 calendar years from 1991 to 2002, which was used to estimate survival for patients with different stages of cancer. The Kaplan-Meier approach was used to extrapolate clinical data to a long-term horizon. A number of simplifying assumptions were also made.

Monetary benefit and utility valuations:
The utility estimates were based on multiple sources, including nationally representative values for the US population and published studies.

Measure of benefit:
The summary benefit measures were the life-years (LYs), disease-free months (DFM) and quality-adjusted life-years (QALYs). These were estimated by combing survival data derived from the model and utility valuations. All benefit measures were discounted at an annual rate of 3%, but undiscounted values were also presented.

Cost data:
The categories of costs included in the analysis were drugs, dual x-ray absorptiometry bone density scans (only for exemestane patients), treatment of local and distant recurrences, and treatment of endometrial cancer and osteoporosis. The drug costs were estimated from the lowest published US average wholesale prices. The costs and resource use associated with cancer recurrence treatment were based on the SEER-Medicare registry. The costs of managing endometrial cancer and osteoporosis were derived from published studies. The price year was 2004 and the costs were in US dollars ($). Given the long timeframe of the analysis, an annual discount rate of 3% was applied.

Analysis of uncertainty:
The issue of uncertainty was addressed by means of probabilistic and deterministic sensitivity analyses. In the former (probabilistic), a non-parametric bootstrapping of patient populations in the IES and SEER-Medicare databases was undertaken in order to generate confidence intervals (CIs) and cost-effectiveness acceptability curves. In the latter (deterministic), plausible ranges of values were considered for key model inputs (base-case value +/- two standard errors or base-case value +/- 25%) in a univariate analysis. In an alternative analysis, data on treatment effects on BC were derived from published sources rather than by extrapolation from the IES database.

Results
The switch to exemestane led to 0.22 additional discounted QALYs (8.77 versus 8.99) and $4,400 additional lifetime costs ($7,724 versus $12,124).

The incremental cost per DFM with exemestane was $680, the incremental cost per LY gained was $13,300, and the incremental cost per QALY gained was $20,100 (95% CI: 12,100 to 59,000).

In patients with HR-positive BC (thus, excluding HR-unknown women), the incremental cost per QALY was even more favourable ($16,600 per QALY).

The cost-effectiveness acceptability curve generated in the probabilistic sensitivity analysis showed that the probability that exemestane is cost-effective was 70.5% at a threshold of $25,000 per QALY and 96.4% at a threshold of $50,000 per QALY.

The deterministic sensitivity analysis showed that the model results were most sensitive to variations in exemestane hazard ratio for distant recurrence, patient utility in the no recurrence state, and the daily cost of exemestane. However, in one of the cases analysed, the incremental cost per QALY for the switching strategy turned out to be higher than $50,000. The use of alternative data for treatment effectiveness improved or worsen the incremental cost-utility results, depending on whether favourable or unfavourable rates for exemestane were used. However, in general, the cost-effectiveness of exemestane remained favourable.

Authors' conclusions
The authors concluded that switching to exemestane after 2 or 3 years of tamoxifen therapy was a cost-effective alternative to continuing on tamoxifen in postmenopausal women with early-stage BC, especially those with HR-positive disease, in the USA.

CRD commentary
Interventions:
The selection of the two therapies was appropriate in that tamoxifen represented the standard of care for this specific patient population, while exemestane was the novel therapy, the economic impact of which had yet to be demonstrated. They are likely to be valid comparators in other settings.

Effectiveness/benefits:
The clinical estimates were derived from a selection of known studies. Specifically, two main sources of data were
used, representing valid databases for the patient population under examination. Therefore, these clinical estimates appear to have been appropriate, although they were not identified through a systematic review of the literature. The use of alternative sources of clinical estimates was appropriate for consideration of the uncertainty surrounding some estimates. Several outcome measures were used and this was a strong feature of the analysis.

Costs:
The authors did not state explicitly which perspective was adopted in the study, although it appears that the cost/resource boundary of the third-party payer might have been adopted. The authors reported the main cost categories, but a detailed breakdown of the cost items was not given. This might limit the possibility of replicating the analysis in other settings. However, the costs of cancer management are often presented in an aggregate fashion. The sources of the costs were reported and appear consistent with the perspective of the payer. Other aspects of the economic analysis, such as the use of discounting and the price year, were reported. The authors noted that the use of the Medicare dataset might limit the generalisability of the study findings, as this specific database considers patients older than 65 years.

Analysis and results:
The synthesis of the costs and benefits was appropriately performed using different benefit measures. A clear description of the decision model in terms of graphical representation, transition patterns and cycle length was provided. The conservative nature of some assumptions should have further strengthened the model results. The issue of uncertainty was satisfactorily addressed, both for the types of analysis considered and for the alternative sources used for treatment effectiveness.

Concluding remarks:
The quality of the study methodology was good. The methods and results were presented clearly and the sensitivity analysis satisfactorily explored some key areas of uncertainty. The authors’ conclusions appear valid and robust.

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Bibliographic details

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Other publications of related interest

Lønning PE. Comparing cost/utility of giving an aromatise inhibitor as monotherapy for 5 years versus sequential administration following 2–3 or 5 years of tamoxifen as adjuvant treatment for postmenopausal breast cancer. Ann Oncol 2006;17:217–25.


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