Pharmacoeconomic analysis of adjuvant therapy with exemestane, anastrozole, letrozole or tamoxifen in postmenopausal women with operable and estrogen receptor-positive 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 objective was to compare the cost-effectiveness of adjuvant therapy with aromatase inhibitors or with tamoxifen in postmenopausal women with operable breast cancer. The authors concluded that exemestane after tamoxifen was more cost-effective than anastrozole or letrozole. The quality of the methodology used was satisfactory. Both the results and methods were adequately reported. As there was no head-to-head comparison of the three aromatase inhibitors, caution should be exercised when evaluating which one was the most cost-effective.

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

Study objective
The objective of the study was to compare the cost-effectiveness of adjuvant therapy with aromatase inhibitors or with tamoxifen in postmenopausal women with operable breast cancer and positive estrogen receptors.

Interventions
The authors made the following head-to-head comparisons:
- exemestane (25 mg/day) versus tamoxifen (20 mg/day) after 2 to 3 years of monotherapy with tamoxifen;
- anastrozole (1 mg/day) versus tamoxifen (20 mg/day) without previous tamoxifen therapy; and
- letrozole (2.5 mg/day) versus placebo after 5 years of monotherapy with tamoxifen.

Location/setting
Spain/secondary care.

Methods
Analytical approach:
A Markov model was used to assess the costs and outcomes of each of the interventions investigated. The time horizon of the analysis was 10 and 20 years. The authors reported that the perspective adopted in the economic analysis was that of the Spanish National Health Care system.

Effectiveness data:
The effectiveness data were derived from published and unpublished data. A literature review of MEDLINE was undertaken to identify all the comparative clinical trials in the area up to May 2005. In addition, the authors consulted various recent reviews of operable breast cancer treatment with tamoxifen, exemestane, anastrozole or letrozole, and a review of all communications presented at several international oncological congresses. All of the effectiveness parameters were then confirmed by expert oncologists and by other similar published models. The main clinical effectiveness estimates were clinical efficacy and toxicity, which were derived from three clinical trials, each with over 1,000 randomised patients.
Monetary benefit and utility valuations:
Quality of life estimates experienced by 63-year-old women with operable breast cancer were derived from published pharmacoeconomic studies.

Measure of benefit:
The measures of benefit were the quality-adjusted life-years (QALYs) and life-years gained.

Cost data:
The authors reported that the costs to the Spanish National Health Care System were included in the analysis. The costs included were those of pharmacological treatment, operable breast cancer recurrence, and complications such as fractures, second neoplasms, deep vein thrombosis, venous thromboembolism, myocardial infarction and stroke. The drug costs were derived from purchasing prices. The costs of complications were derived from diagnosis-related groups or the patient management categories, which were obtained from a Spanish costs database. The costs of breast cancer recurrence were obtained from two Spanish clinical practice guides. The price year was 2004. The costs were expressed in euros (EUR). Since the costs could be incurred over a period of up to 20 years, discounting was performed at an annual rate of 3.5%.

Analysis of uncertainty:
To assess the stability and consistency of the results, a series of one-way sensitivity analyses was performed. These considered the minimum and maximum cost estimates and variations in the discount rate.

Results
Over a 20-year time horizon, the average additional life-years gained ranged from 1.046 to 1.312 when exemestane was compared with tamoxifen, and were 0.535 when anastrozole was compared with tamoxifen and 0.899 when letrozole was compared with placebo.

Over a 20-year time horizon, the average additional QALYs gained ranged from 0.566 to 0.708 when exemestane was compared with tamoxifen, and were 0.285 when anastrozole was compared with tamoxifen and 0.474 when letrozole was compared with placebo.

Over a 20-year time horizon, the average incremental costs ranged from EUR 20,020 to EUR 20,425 when exemestane was compared with tamoxifen, and were EUR 17,806 when anastrozole was compared with tamoxifen and EUR 23,444 when letrozole was compared with placebo.

The costs and benefits were combined using an incremental cost-effectiveness ratio (ICER; the additional cost per life-year gained) and an incremental cost-utility ratio (ICUR; the additional cost per QALY gained). The ICER was between EUR 15,568 and EUR 19,139 when exemestane was compared with tamoxifen, and was EUR 33,282 when anastrozole was compared with tamoxifen and EUR 26,078 when letrozole was compared with placebo. The ICUR was between EUR 28,849 and EUR 35,371 when exemestane was compared with tamoxifen, and was EUR 62,477 when anastrozole was compared with tamoxifen and EUR 49,460 when letrozole was compared with placebo.

The results of the one-way sensitivity analyses showed that the results were consistent with those observed in the base-case when the costs were varied and when discounting was not performed.

Authors' conclusions
The authors concluded that treatment with exemestane after tamoxifen was more cost-effective than treatments with anastrozole or with letrozole.

CRD commentary
Interventions:
Appropriate details of the interventions were reported. The justification for using tamoxifen as the comparator was that it is an effective treatment, and that it was used for the control arm in two of the three trials included in the review. Placebo was chosen as the comparator for letrozole because, in the only large clinical trial identified, placebo was the control arm.
Effectiveness/benefits:
The authors reported that relevant literature was identified through a systematic review of MEDLINE. Consequently, relevant studies not indexed under MEDLINE could have been missed. However, the authors also identified other published and unpublished literature by reviewing recent reviews of the literature and abstracts presented at international oncological conferences. In addition, clinical estimates used to populate the model were reviewed by expert oncologists and compared with those used in other published pharmacoeconomic models. Appropriate details on how quality of life estimates were derived were also reported.

Costs:
The perspective adopted in the economic analysis was clearly reported to have been that of the health care system. Given this perspective, all relevant major costs appear to have been included. The authors appropriately reported the sources from which costs were derived, the price year used, the time horizon and the discount rate.

Analysis and results:
Appropriate details of the Markov model used to synthesise cost and outcome data were reported, along with a graphical depiction of the model. Uncertainty in the model was only assessed by varying the cost parameters and not the effectiveness parameters. In addition, the use of probabilistic sensitivity analyses is a more thorough way in which to assess overall model uncertainty. In general, both the results and methods were adequately reported. In their analysis, the authors did not compare the different interventions head-to-head. For example, anastrozole was not compared head-to-head with exemestane. As a result, caution should be exercised when deciding which of the three aromatase inhibitors (i.e. anastrozole, exemestane or letrozole) was the most cost-effective. The authors highlighted the limitations of their study in the conclusion.

Concluding remarks:
Overall, the quality of the methodology used was satisfactory. Both the results and methods were adequately reported. As there was no head to head comparison of the three aromatase inhibitors under study, caution should be exercised when evaluating which one was the most cost-effective.

Funding
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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Androstadienes /economics /therapeutic use; Antineoplastic Agents, Hormonal /economics /therapeutic use; Aromatase Inhibitors /economics /therapeutic use; Breast Neoplasms /chemistry /drug therapy /economics /surgery; Chemotherapy, Adjuvant /economics; Cohort Studies; Computer Simulation; Cost-Benefit Analysis; Estrogen Antagonists /economics /therapeutic use; Estrogens; Fees, Pharmaceutical; Female; Follow-Up Studies; Humans; Markov Chains; Middle Aged; Models, Theoretical; Neoplasm Proteins /analysis; Neoplasms, Hormone-Dependent /chemistry /drug therapy /economics /surgery; Nitriles /economics /therapeutic use; Postmenopause; Quality-Adjusted Life Years; Randomized