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 objective was to compare ixabepilone plus capecitabine with capecitabine alone in patients with advanced breast cancer, who were resistant to taxanes and previously treated with or resistant to an anthracycline. The cost of ixabepilone and its incremental cost-effectiveness ratios were higher than those for other treatments for advanced breast cancer. The reliability of the data collected after treatment ended was limited, but the authors' conclusions were appropriate, provided these data were the best clinical evidence available.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to compare ixabepilone plus capecitabine with capecitabine alone in patients with advanced breast cancer, who were resistant to taxanes and were previously treated with or resistant to an anthracycline.

Interventions
The interventions were ixabepilone 40mg per m$^2$ on day one, plus capecitabine 2g per m$^2$ per day for the first 14 days of each 21-day cycle, compared with capecitabine 2.5g per m$^2$ per day for the first 14 days of each 21-day cycle.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A decision tree was used to model four levels of response to treatment, which were linked to survival curves for progression-free survival and overall survival. The survival data were from a single clinical study. The model had a lifetime horizon and the authors reported a health care system perspective.

Effectiveness data:
The clinical effectiveness data were from a randomised controlled trial that included women with locally advanced or metastatic breast cancer that was resistant to taxanes and had previously been treated with or was resistant to an anthracycline. After recruiting 377 patients the definition of taxane resistance was amended and a total of 752 patients were randomly assigned to treatment. The details of this study were reported elsewhere (Thomas, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details).

Monetary benefit and utility valuations:
The utility estimates were applied to patients in four health states and were derived from the clinical trial. They were measured using the Health Utilities Index Mark 3 (HUI3). During active treatment, the utility values varied according to the treatment regimen and the level of response.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained and these were discounted at a rate of 3% per year, starting from the second month.
Cost data:
The analysis included the costs of drugs, in-patient care, out-patient care, emergency department care, home health visits, and diagnosis. The currency was US dollars ($) and the price year was 2008. Costs were discounted at 3% per year, from the second month.

Analysis of uncertainty:
Probabilistic sensitivity analysis was performed, using Monte Carlo simulation.

Results
Total (undiscounted) costs for patients receiving ixabepilone plus capecitabine were $60,900 compared with $30,000 for patients receiving capecitabine alone. The estimated gain in life expectancy with the addition of ixabepilone was 1.96 months (95% CI 1.36 to 2.64) and the estimated gain in quality-adjusted survival was 1.06 months (95% CI 0.09 to 2.03). With discounting, the estimated incremental cost-effectiveness ratio (ICER) for patients receiving ixabepilone plus capecitabine was $193,000 per life-year saved and $359,000 per QALY.

In all sensitivity analysis analyses the ICER remained greater than $100,000 per life-year saved and $150,000 per QALY. Increases in medical resource use or costs incurred after treatment discontinuation led to higher ICER’s. The results were most sensitive to the choice of survival analysis technique, with estimates generated from the exponential model resulting in an ICER of $108,000 per life-year saved and $187,000 per QALY.

Authors’ conclusions
The authors concluded that the cost of ixabepilone and its incremental cost-effectiveness ratios were higher than those for other treatments for advanced breast cancer.

CRD commentary
Interventions:
Both interventions were described briefly and the usual care was also described.

Effectiveness/benefits:
The efficacy data were from a clinical trial, in which, during the recruitment period, the definition of taxane resistance was amended. The authors noted that there were no follow-up data beyond the date of progression for patients who had survived and many patients did not complete the utility questionnaire after the end of the treatment. The effect of this was unclear. They reported no literature review to identify the efficacy and utility data, which makes it impossible to ascertain if the best available evidence was used.

Costs:
The authors reported a health care system perspective and they included all of the relevant costs. They noted that the medical resource use data were collected only once, at the end of treatment, and they might have been underestimated. The unit costs for these resources were reported, as was the discounting of costs.

Analysis and results:
The analytical approach and the results were satisfactorily reported. The model structure was described, with a diagram, and the parameter uncertainty was appropriately assessed. The authors discussed the limitations of their study.

Concluding remarks:
The reliability of the data collected after treatment ended was limited, but the authors’ conclusions were appropriate, as long as the trial provided the best clinical evidence available.

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Other publications of related interest

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Subject indexing assigned by NLM

MeSH
Anthracyclines /therapeutic use; Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Breast Neoplasms /drug therapy /mortality /pathology; Bridged Compounds /therapeutic use; Capecitabine; Cost-Benefit Analysis; Deoxycytidine /administration & dosage /analogs & derivatives; Disease Progression; Drug Costs; Drug Resistance, Neoplasm; Epothilones /administration & dosage; Female; Fluorouracil /administration & dosage /analogs & derivatives; Humans; Neoplasm Metastasis; Quality-Adjusted Life Years; Taxoids /therapeutic use

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