Cost effectiveness of treatment options in advanced breast cancer in the UK
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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.

Health technology
The use of three chemotherapeutic treatments for patients with advanced breast cancer. The treatments were docetaxel (taxoid), paclitaxel (taxoid), and vinorelbine (vinca alkaloid). Docetaxel (one-hour infusion) and paclitaxel (three-hour infusion) were administered as a single dose every 3 weeks for a total of 6 chemotherapy cycles. Vinorelbine was administered weekly for a total of 12 chemotherapy cycles.

Type of intervention
Chemotherapeutic treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised women requiring chemotherapeutic treatment for anthracycline-resistant advanced breast cancer. Further inclusion and exclusion criteria were not given since the authors stated that a typical patient was difficult to define, due to the highly complex nature of the disease and its treatment.

Setting
The setting was a hospital. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness evidence was mainly derived from a study published in 2000 (see Other Publications of Related Interest). The cost data were converted into 1997 to 1998 prices, whereas the drug costs referred to 1999.

Source of effectiveness data
The effectiveness evidence was derived from a systematic review of published studies (see Other Publications of Related Interest), and was supported by the authors' assumptions.

Modelling
A Markov decision analytic model was used to simulate the typical course of the treatment of a patient with advanced breast cancer through discrete disease states and toxicities. The overall timeframe of the model was 3 years from the initiation of the salvage therapy and the length of each cycle was 3 weeks. After each course of treatment, the patient had complete response, partial response, stable disease, or progressive disease. The overall response rate was calculated by combining the complete and partial responses. The model also took into account immediate (nausea and vomiting), intercurrent (neutropenia) or cumulative (severe fluid retention, severe peripheral neuropathy, arthralgia, myalgia, and skin conditions) toxicities resulting from chemotherapy.
Outcomes assessed in the review
The outcomes assessed in the review were the overall response rate, time to progression, median survival, time to response, courses of chemotherapy, and the probabilities for the following:

- progressive disease,
- infection with hospitalisation and/or intravenous antibacterials,
- febrile neutropenia with hospitalisation,
- neutropenia without hospitalisation,
- death associated with infection or febrile neutropenia,
- severe neurotoxicity,
- severe oedema,
- severe skin condition, and
- severe nail condition.

Study designs and other criteria for inclusion in the review
The effectiveness data were derived from a systematic review of randomised controlled trials.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
The effectiveness evidence was derived from a systematic review of eleven primary studies.

Methods of combining primary studies
Weighted averages were calculated to combine the effectiveness estimates derived from the primary studies.

Investigation of differences between primary studies
Not carried out.

Results of the review
The overall response rate was 41.7% with docetaxel, 28% with paclitaxel, and 16% with vinorelbine.

The time to progression was 24 weeks with docetaxel, 21 weeks with paclitaxel, and 12 weeks with vinorelbine.
The median survival was 56 weeks with docetaxel, 46 weeks with paclitaxel, and 36 weeks with vinorelbine.

The time to response was 9 weeks with both docetaxel and paclitaxel, and 6 weeks with vinorelbine.

There were 6 courses of chemotherapy with docetaxel and paclitaxel, and 12 with vinorelbine.

The probability values were:

- 23.8% with docetaxel, 21% with paclitaxel, and 38.4% with vinorelbine for progressive disease;
- 8.8% with docetaxel, 4% with paclitaxel, and 10% with vinorelbine for infection with hospitalisation and/or intravenous antibacterials;
- 7.3% with docetaxel, 7% with paclitaxel, and 0 with vinorelbine for febrile neutropenia with hospitalisation;
- 10.7% with docetaxel, 10% with paclitaxel, and 0 with vinorelbine for neutropenia without hospitalisation;
- 1.2% with docetaxel, and 0 with paclitaxel and vinorelbine for death associated with infection or febrile neutropenia;
- 5% with docetaxel, 9% with paclitaxel, and 2% with vinorelbine for severe neurotoxicity;
- 4% with docetaxel, and 0 with paclitaxel and vinorelbine for severe oedema;
- 3% with docetaxel, and 0 with paclitaxel and vinorelbine for severe skin condition; and
- 3.4% with docetaxel, and 0 with paclitaxel and vinorelbine for severe nail condition.

**Methods used to derive estimates of effectiveness**

The authors made some assumptions used in the decision model.

**Estimates of effectiveness and key assumptions**

The model assumed that:

- all patients achieving response received the full drug dose;
- cumulative conditions persisted for 9 weeks;
- patients who responded to the treatment had a better quality of life than patients who progressed;
- patients who experienced an adverse effect from therapy had a reduced quality of life at that time and incurred additional costs;
- treatment response would be evident by the second cycle and confirmed by the fourth cycle;
- patients who progressed at cycle 2 were withdrawn from therapy and developed early progressive disease;
- patients with a response or stable disease proceeded through cycle 3 to cycle 4 when the response was confirmed;
- patients who did not withdraw from therapy because of severe cumulative toxicities completed the course of treatment, and remained in the response or stable disease states for the median duration of response, and then developed progressive disease.

**Measure of benefits used in the economic analysis**

The benefit measure used in the economic analysis was the quality-adjusted life-years (QALYs). Utility values were

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derived, using the standard gamble technique, from a sample of 30 oncologist nurses from specialist cancer centres in the UK and from 150 nurses in four other Western European countries.

**Direct costs**
A 6% discount rate was used for those costs that were incurred after the first year, as recommended by the UK Treasury. The unit costs were reported and a complete breakdown of the costs was given. The cost/resource boundary adopted was that of the NHS. The cost analysis included the drugs, chemotherapy administration, (regular or intensive care) hospital stay, general practitioner consultation, and specialist consultation. The overall costs of specific health states were also included, such as early progressive disease, late progressive disease, stable disease, terminal disease, neutropenia, severe neurotoxicity, and severe oedema. Five oncologists, who defined the overall treatment pattern, estimated the quantities of the resources used in the decision model. The unit costs were estimated using actual data from national databases. The NHS Hospital and Community Inflation Index was used to convert these costs into 1997 to 1998 prices. The drug costs referred to 1999 prices.

**Statistical analysis of costs**
No statistical analysis of the costs was carried out.

**Indirect Costs**
The indirect costs were not included, as they were irrelevant to the perspective adopted in the study.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
One-way sensitivity analyses were carried out to assess the effect of a number of variables on the robustness of the model and the estimated cost-utility ratios. The effect of variations in the discount rates (both benefits and costs were discounted at 6%), utility values used to calculate the QALYs, costs applied to disease states and toxicities experienced, were investigated.

**Estimated benefits used in the economic analysis**
In the comparison between docetaxel and paclitaxel, the number of QALYs gained was 0.7347 with docetaxel and 0.6485 with paclitaxel. Consequently, docetaxel resulted in 0.0862 extra QALYs, equivalent to 31 days of perfect health, over paclitaxel.

In the comparison between docetaxel and vinorelbine, the number of QALYs gained was 0.7347 with docetaxel and 0.4822 with vinorelbine. Thus, docetaxel resulted in 0.2525 extra QALYs, equivalent to 92 days of perfect health, over vinorelbine.

**Cost results**
In the comparison between docetaxel and paclitaxel, the total costs were 7,817 with docetaxel and 7,645 with paclitaxel. Docetaxel therefore resulted in an extra cost of 172 over paclitaxel.

In the comparison between docetaxel and vinorelbine, the total costs were 7,817 with docetaxel and 4,268 with vinorelbine. Hence, docetaxel resulted in an extra cost of 3,549 over vinorelbine.

**Synthesis of costs and benefits**
The costs and the benefits were combined in an incremental cost-utility analysis. The incremental cost per QALY
gained with docetaxel over paclitaxel was 1,995, while that for docetaxel over vinorelbine was 14,055. In the sensitivity analyses, the maximum cost/QALY for docetaxel versus paclitaxel was 6,055 (cost of progressive disease reduced to 100 per 3-week period). For docetaxel versus vinorelbine, the maximum cost/QALY was 15,095 (utility values for disease states pooled from 6 countries).

Authors’ conclusions
"The results demonstrated that docetaxel is a cost-effective therapy for use in patients with advanced breast cancer when compared with vinorelbine.”

CRD COMMENTARY - Selection of comparators
The authors justified the selection of the three treatments studied in the paper. All represented treatment choices and commonly used salvage chemotherapy options licensed in the UK. You should assess whether they are currently used in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis mainly used a systematic review of published studies. Weighted averages were used to combine the effectiveness evidence derived from the primary studies, which were based on randomised designs. Details of the methodology of the review may be found in the original study. The authors made several assumptions to support the data derived from the literature. However, only a few of these assumptions were tested in the sensitivity analysis. The authors pointed out that the result of the analysis should be interpreted with caution, due to the lack of head-to-head comparisons among the drugs included in the analysis, and because of differences among the primary studies in terms of the patient populations and clinical outcomes.

Validity of estimate of measure of benefit
QALYs were used as a summary benefit measure. These were derived from a decision model, which was explicitly described and which appropriately simulated the natural management of the patients included in the analysis. The benefit was not discounted in the base-case, but was in the sensitivity analyses, where the validity of the utility values used was also tested.

Validity of estimate of costs
All the categories of costs relevant to the perspective adopted in the study were included in the economic analysis. A complete breakdown of the costs was given and the unit costs were reported, thus enhancing transparency and facilitating generalisability. The costs were generally inflated to 1997 to 1998 prices, whereas the drug costs were estimated at 1999 prices. No statistical analysis of the costs or quantities was carried out, but a few sensitivity analyses were performed. The quantities were estimated on the basis of expert opinion. The costs arising from differences in the administration schedules were not included in the analysis. The authors stated that those costs would increase the expenses associated with paclitaxel more than those associated with docetaxel. As a result, the overall study conclusions were not affected by this omission or by the exclusion of the indirect costs.

Other issues
The authors compared their findings with those from other studies and the results were similar. The issue of the generalisability of the study results to other settings was not explicitly addressed, but some sensitivity analyses were carried out. The results of these were reported in detail, thus enhancing the external validity of the analysis. The study population comprised patients with advanced breast cancer, and this was reflected in the conclusions of the analysis. The authors reported some limitations of their study. These were mainly related to the effectiveness estimates.

Implications of the study
On the basis of effectiveness, the results of the analysis support the use of docetaxel in the treatment of advanced breast
cancer, over paclitaxel or vinorelbine. The docetaxel-based treatment would be "strongly recommended", based on the criteria for making evidence-based decisions in the UK. The authors suggested that the use of patient-derived utility values to calculate the QALYs would strengthen the decision model. While the authors state that docetaxel is cost-effective, it should be noted that this depends on the opportunity cost of its use. Since docetaxel was shown to cost more than the other drugs, the gain in utility (QALYs) for this extra cost needs to be compared with the loss that might be produced by a re-allocation of resources within a fixed budget. From the perspective of the UK NHS, this would be by reallocation within the NHS budget.

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**Other publications of related interest**

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