Costs and consequences of using pamidronate compared with zoledronic acid in the management of breast cancer patients in the UK
Guest J F, Clegg J P, Davie A M, McCloskey E

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
Two bisphosphonates for the prophylaxis of morbidity due to metastatic bone disease in women with breast cancer were examined. These were pamidronate (90 mg/infusion every 3 to 4 weeks) and zoledronic acid (4 mg/infusion every 3 to 4 weeks).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 18 years or older with breast cancer, who were receiving antineoplastic therapy and who had at least one bone metastasis (lytic or mixed). The study population referred to both patients on chemotherapy and patients on hormone therapy.

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

Dates to which data relate
The effectiveness data were derived from a study published in 2001. No dates were explicitly reported for the resource use data. The costs were assessed using 2003/2004 prices.

Source of effectiveness data
The effectiveness evidence was derived from a single study that was identified from a review of the literature.

Modelling
A decision tree model was constructed to assess the expected direct health care costs 12 months after initiating bisphosphonate treatment for the prophylactic management of skeletal morbidity. The model considered two subgroups of women, those on chemotherapy and those on hormone therapy. Women receiving either zoledronic acid or pamidronate could develop skeletal-related events (SREs) or non-SREs without hypercalcaemia, and then either continue treatment for one year or discontinue it. Patients who did not continue with their initial bisphosphonate for 12 months were deemed to have discontinued bisphosphonate treatment, in accordance with experts' opinions. The structure of the tree was reported.
Outcomes assessed in the review
The outcomes assessed from the literature were:

the proportion of patients with at least one SRE,
the time to the first SRE,
the number of SREs at 12 months, and
the discontinuation rates with pamidronate and zoledronic acid.

Study designs and other criteria for inclusion in the review
A systematic literature search was undertaken to identify primary estimates on skeletal morbidity in breast cancer. Only English language papers were included. Other search criteria were not reported.

Sources searched to identify primary studies
MEDLINE, EMBASE, TRIP, Current Contents, NHS EED and Cochrane databases were searched. A manual search was also performed.

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
One primary study provided the data.

Methods of combining primary studies
Not relevant since only one study was used.

Investigation of differences between primary studies
Not relevant.

Results of the review
The proportion of patients with at least one SRE and time to first SRE were similar (not significantly different) in both treatment groups at 12 months. In particular, the probability of SREs was 0.43 for pamidronate and 0.44 for zoledronic acid for patients on chemotherapy, and 0.47 (pamidronate) and 0.42 (zoledronic acid), respectively, for patients on hormone therapy.

The number of SREs was similar in both treatment groups at 12 months.

In the sub-group of patients on chemotherapy, the incidences of SREs with pamidronate versus zoledronic acid were:

for non-vertebral fracture, 1.05 and 0.93;
for vertebral fracture, 0.63 and 0.61;
for spinal cord compression, 0.21 and 0.07;
for radiotherapy to bone, 1.65 and 1.07; and
for bone surgery, 0.23 and 0.11.

In the sub-group of patients on hormone therapy, the incidences of SREs with pamidronate versus zoledronic acid were:
for non-vertebral fracture, 0.96 and 0.98;
for vertebral fracture, 0.57 and 0.64;
for spinal cord compression, 0.19 and 0.07;
for radiotherapy to bone, 1.51 and 1.12; and
for bone surgery, 0.21 and 0.12.

In the sub-group of patients on chemotherapy, the discontinuation rate after 1 year was 0.61 for both pamidronate and for zoledronic acid in the case of no SREs, and 0.09 (pamidronate) and 0.07 (zoledronic acid), respectively, in the case of SREs.

In the sub-group of patients on hormone therapy, the discontinuation rate after 1 year was 0.66 for pamidronate and 0.59 for zoledronic acid in the case of no SREs, and 0.08 (pamidronate) and 0.07 (zoledronic acid), respectively, in the case of SREs.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis since no statistically significant difference was observed between the groups. In effect, a cost-minimisation analysis was performed.

Direct costs
The cost analysis was carried out from the perspective of the NHS. The health services included in the economic evaluation were bisphosphonate therapy, outpatient visits, diagnostic tests, and resources associated with SREs (hypercalcaemia, non-vertebral fracture, vertebral fracture, spinal cord compression, radiotherapy to bone and bone surgery). The unit costs and the quantities of resources used were presented separately. Resource use was derived from a survey of a randomly selected sample of eight consultant oncologists and seven breast cancer nurses from across the UK, using interviews based on a structured questionnaire. The questionnaire focused on patient management, the treatment of SREs and the associated resources. The costs were estimated from the NHS Reference Cost database at 2003/2004 prices. The panel also estimated the average time attributable to an infusion. Discounting was not relevant since costs were incurred during one year.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
UK pounds sterling (£).
Sensitivity analysis
A probabilistic sensitivity analysis (Monte Carlo simulation with 1,000 iterations of the model) was used to simultaneously vary probabilities, resource use values and clinical outcomes within the model. The probabilistic distributions that were assigned to each group of inputs were reported (beta distributions for probabilities and log-normal for resource use). Further, a two-way sensitivity analysis was carried out to identify how the incremental cost of one treatment relative to the other would change by varying different parameters in the model. A multivariate sensitivity analysis on infusion times was also performed. The authors appear to have set the ranges of values used.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
In the sub-group of patients receiving chemotherapy, the expected costs over one year were 6,045.52 with pamidronate and 6,981.39 with zoledronic acid.

In the sub-group of patients receiving hormone therapy, the expected costs over one year were 5,400.67 with pamidronate and 6,043.43 with zoledronic acid.

Thus, the use of pamidronate led to an 11 to 13% reduction in health care costs over the first year of treatment, which was primarily due to the lower acquisition cost of pamidronate and fewer tests among pamidronate-treated patients.

The probabilistic sensitivity analysis showed that 78% and 70% of a cohort of pamidronate-treated patients on chemotherapy and hormone therapy, respectively, would be expected to cost less than zoledronic acid-treated patients. Such variation was primarily due to the variability around the probability of completing 12 months of treatment with zoledronic acid.

The two-way sensitivity analysis on selected pairs of model inputs suggested that the base-case results were robust to variations in the model inputs.

The budget impact analysis assumed that the ratio of patients suffering from breast cancer who received chemotherapy and hormone therapy was 2:3. The results of this analysis showed that treating a cohort of between 100 and 500 women with breast cancer with pamidronate instead of zoledronic acid could potentially reduce NHS management costs by between 77,000 and 386,000.

The average time attributable to an infusion was approximately 20 minutes shorter with pamidronate than with zoledronic acid. The primary driver of time among pamidronate-infused patients was found to be administration and infusion. This accounted for at least 60% of the total time attributable to an infusion. In contrast, the primary drivers of time among zoledronic acid-infused patients were found to be pre-infusion tests and waiting for these test results. These collectively accounted for at least 60% of the total time attributable to an infusion. The Monte Carlo simulations showed that in 68% of a cohort of pamidronate-infused patients, the infusion would be expected to take less time than in patients infused with zoledronic acid.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-minimisation analysis was carried out.

Authors' conclusions
Pamidronate was the preferred strategy for breast cancer patients who were receiving antineoplastic therapy and who had at least one bone metastasis (lytic or mixed).

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparators was clear. The authors discussed the treatments available for the management of skeletal morbidity in women with breast cancer. The choice of the two bisphosphonates was appropriate. Dosages were reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a review of the literature. Most aspects of the conduct of the review were reported. No strict inclusion criteria were used. However, only one study was found that directly compared the two drugs, thus clinical data came from a single study, which was a clinical trial. No information on the characteristics of the patients or other features of the design was provided, but the use of a trial ensures a high internal validity. The authors stated that many clinical inputs were derived from values that did not distinguish between breast cancer and multiple myeloma patients, and this might limit the appropriateness of some data. The uncertainty around the clinical parameters was extensively addressed in the sensitivity analyses.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The costs included were consistent with the perspective adopted in the study. Only the direct medical costs were considered in the study. A detailed breakdown of the cost items was reported, and the unit costs were presented separately from the quantities of resources used. This enhances the possibility of replicating the results of the analysis in other settings. The costs were treated deterministically in the base-case, but extensive sensitivity analyses were performed. The costs were estimated from typical NHS sources. The price year was reported, thus aiding reflation exercises in other time periods. The impact of individual cost components was reported.

Other issues
The authors compared their results with those from other published studies. Since contrasting results had been reported in the literature (depending on the characteristics of the studies), the current study was consistent with the findings of some studies and conflicting with the results of others. However, it was noted that limited studies on the economic evaluation of the two bisphosphonates were available. The issue of the generalisability of the study results to other settings was not explicitly addressed, but extensive sensitivity analyses were performed. These increase the external validity of the study. The results of the analysis were reported clearly and extensively. The authors noted that some costs (i.e. those borne by the patients), as well as the impact of the interventions on quality of life, were not considered in the analysis. This represents a further limitation of the study.

Implications of the study
The study results support the use of pamidronate for breast cancer patients who are receiving antineoplastic therapy and who have at least one bone metastasis (lytic or mixed).

Source of funding
Sponsored financially by Mayne Pharma.

Bibliographic details

PubMedID
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Antineoplastic Agents /economics /therapeutic use; Breast Neoplasms /drug therapy /physiopathology; Calcium Metabolism Disorders /economics /prevention & control; Chemoprevention; Cost-Benefit Analysis; Decision Support Techniques; Diphosphonates /economics /therapeutic use; Female; Great Britain; Health Care Costs; Humans; Imidazoles /economics /therapeutic use; Middle Aged; State Medicine /economics

AccessionNumber
22005000912

Date bibliographic record published
28/02/2006

Date abstract record published
28/02/2006