Zoledronic acid versus pamidronate: cost minimisation in bone metastasis

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 treatments compared were intravenous (iv) infusions of 90 mg pamidronate and 4 mg zoledronic acid in the adjunct treatment of bone metastasis in patients with breast cancer and multiple myeloma. Both treatments were administered at intervals of 4 weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with multiple myeloma in Stage III of Durie-Salmon or with advanced breast cancer and at least one bone lesion.

Setting
The study setting was secondary care. The economic study was undertaken in Spain.

Dates to which data relate
The effectiveness data were derived from a study published in 2001. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a single study (Rosen et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details).

Link between effectiveness and cost data
The costing was undertaken retrospectively and was not based on the patient sample used for the effectiveness data.

Study sample
The effectiveness data were derived from the study by Rosen et al. (2001). Consequently, the authors only presented brief details of this study. A total of 1,648 patients participated in the trial. These patients received treatment for 12 months with either zoledronic acid or pamidronate, both administered through iv infusion.

Study design
The study was a multi-centre, randomised, double-blind clinical trial with double dummy. The duration of follow-up
was 12 months.

Analysis of effectiveness
The primary outcome measured in the trial was the percentage of patients who presented at least one skeletal-related event (SRE), excluding hypercalcaemia of malignancy. An SRE was taken to mean the presence of pathological fractures, spinal cord compression, or the need for bone radiotherapy or surgery. Secondary variables were the proportion of patients experiencing any SRE, the time lapse until the first SRE, the skeletal morbidity rate, and the incidence of bone radiotherapy.

Effectiveness results
The study found that the percentage of patients treated in clinical trials with either zoledronic acid or pamidronate who presented at least one SRE during the first year of treatment was similar in the two groups.

Zoledronic acid was found to significantly reduce the incidence of bone radiotherapy from 0.71 to 0.47 therapies per patient per year, (p=0.018).

Clinical conclusions
The study found no statistically significant differences between the two treatments in the primary outcome measure.

Measure of benefits used in the economic analysis
The authors demonstrated therapeutic equivalence between the two treatments and only analysed costs in the economic analysis.

Direct costs
The direct costs included in the analysis were those to the health care provider. These comprised costs incurred during the administration of the drugs and those related to the radiotherapy sessions avoided by each treatment. The costs incurred during drug administration covered the drugs, patient monitoring during iv infusions, disposables and occupation of infusion chairs. Data on the consumption of health care resources for the infusion of the study drugs were collected through a semi-structured questionnaire, administered to the managers of oncology infusion sites at seven Spanish hospitals. The questionnaire asked about the times that patients occupied an infusion chair during treatment sessions and the time health care staff dedicated to the preparation, administration, monitoring and finalisation of the iv infusion. Data from clinical trials were used to estimate the number of radiotherapy treatments needed for patients treated with each drug.

The study drugs were valued according to their ex-factory price. All other administration-related resources were valued using internal costs from a local health care cost database. Radiotherapy costs were derived from data obtained from a Spanish study that analysed the costs incurred by hospitals for different radio therapeutic services. Discounting was not relevant, as the costs were incurred during one year, and was therefore appropriately not performed. The study reported the incremental costs. The price year was 2002.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included.

Currency
Sensitivity analysis
One-way sensitivity analyses were undertaken by varying one parameter at a time. The parameters investigated were the incidence of radiotherapy, the number of treatment sessions, personnel time, and the cost of radiotherapy.

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

Cost results
The additional costs of zoledronic acid in comparison with pamidronate were EUR 134.92 per patient per year. This was equivalent to 5.1% of the current drug cost of a treatment with pamidronate.

The results of the sensitivity analyses showed that a change in parameters such as the incidence of radiotherapy, the number of treatment sessions, personnel time, and the cost of the radiotherapy, did not vary the authors' results, as under these varying scenarios pamidronate was still associated with cost-savings in comparison with zoledronic acid. The cost-savings ranged from EUR 195.27 to EUR 253.39 per patient.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Savings due to the shorter infusion time and the better outcomes of zoledronic acid in avoiding palliative radiotherapy could almost completely compensate for its higher acquisition cost in comparison with pamidronate.

CRD COMMENTARY - Selection of comparators
A justification was given for using pamidronate infusions as the comparator. Pamidronate represents one of the two most commonly used bisphosphonates in oncology. You should decide if this represents a widely used treatment in your own setting.

Validity of estimate of measure of effectiveness
There were insufficient details of the trial used to derive effectiveness measures for one to be able to comment on its quality. However, as the trial was based on a multi-centre, randomised, double-blind clinical trial with double dummy and had a large study sample (over 1,500 patients), it is very likely that the results from this trial were internally valid.

Validity of estimate of measure of benefit
The authors demonstrated therapeutic equivalence between the two treatments and only analysed costs in the economic analysis.

Validity of estimate of costs
All the categories of cost relevant to the perspective of the health care provider were included in the analysis. Further, it appears that no major relevant costs have been omitted from the analysis. The costs and the quantities were reported separately, which will enhance the generalisability of the authors' results. Resource use was mainly derived from a questionnaire, which was administered to managers of oncology sites at seven Spanish hospitals. A one-way sensitivity analysis of resource use was performed, although the sensitivity analysis does not appear to have been conducted over a wide range of values. The unit costs were derived from a local health care database. Only one unit cost (occupation of
an infusion chair) was varied in the sensitivity analysis. Again, the range of values used would not appear to have been wide enough. Since all the costs were incurred during a one-year period, discounting was unnecessary and was therefore not performed. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors reported that their results on the time needed to prepare, administer and monitor the infusions was similar to the results found in an American study, which also found that in the time it took to treat one patient with pamidronate, on average more than three patients could be treated with zoledronic acid. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, but their conclusions did not reflect their results. The authors undertook a cost-minimisation analysis because no major differences were found in terms of effectiveness between the two interventions. However, in their conclusions they reported better outcomes for zoledronic acid in avoiding palliative radiotherapy. If the authors believed this was an important outcome measure, they should have used a cost-effectiveness analysis and derived the incremental cost per palliative radiotherapy treatment avoided when zoledronic acid is compared with pamidronate. Further, the authors found that pamidronate generated cost-savings of approximately EUR 134.92 per person per year, which the authors implied was virtually negligible. However, this was a subjective opinion, and if many patients were offered zoledronic acid the financial impact on the health care system could be significant. Also, in the cost-minimisation analysis, the treatment with the lowest costs is normally the treatment recommended for use. The authors reported no limitations to their study.

Implications of the study
The authors recommended that a prospective, naturalistic and representative study of the oncology settings in Spain should be undertaken to verify the results of this analysis.

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Funded by Novartis Oncology.

Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
Bone Neoplasms /prevention & control /drug therapy; Breast Neoplasms; Clinical Trials as Topic; Cost-Benefit Analysis; Costs and Cost Analysis; Diphosphonates; Double-Blind Method; Drug Costs; Fatigue; Fever; Health Care Costs; Health Services; Hypercalcemia /prevention & control /drug therapy; Multicenter Studies as Topic; Multiple Myeloma; Nausea; Nurses; Pain; Palliative Care; Radiotherapy; Randomized Controlled Trials as Topic; Treatment
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