Cost-effectiveness of zoledronic acid in the management of skeletal metastases in patients with lung cancer in France, Germany, Portugal, the Netherlands, and the United Kingdom

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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.

CRD summary
This study examined the cost-effectiveness of zoledronic acid to reduce the risk of new skeletal events in patients with non-small cell lung cancer and bone metastases, from the perspective of the national health service. The authors concluded that zoledronic acid was cost-saving or cost-effective compared with placebo in France, Germany, the UK, Portugal, and the Netherlands. The cost-effectiveness methods were appropriate, which should make the authors’ conclusions valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of zoledronic acid to reduce the risk of new skeletal events in patients with non-small cell lung cancer (NSCLC) and bone metastases.

Interventions
Zoledronic acid (4mg every three weeks), administered as a 15-minute infusion, was compared with placebo. The treatment was given for up to 21 months.

Location/setting
France, Germany, Portugal, Netherlands, and UK/hospital.

Methods
Analytical approach:
The model was a computer simulation, with a short time horizon. The authors stated that the perspective of the national health care system was adopted.

Effectiveness data:
The treatment effect and drug safety data were from a published phase III, double-blind, randomised controlled trial (RCT), of 124 patients with NSCLC who received zoledronic acid and 120 patients who received placebo. These patients were initially followed-up for nine months, with a further 12-month follow-up conducted in an extension study to establish the long-term treatment efficacy. The rate of skeletal events was the primary endpoint of the trial.

Monetary benefit and utility valuations:
The utility values were from a published study that used the European Quality of life (EQ-5D) instrument to elicit the preferences. The duration of the disutility due to skeletal events was from another published study.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of zoledronic acid, its administration, disposable supplies, labour, and the treatment of skeletal events. The costs and resource quantities were from country-specific sources. Specifically, cost-of-illness studies were used for the Netherlands and Portugal, while for France, Germany, and the UK the data were...
estimated, using diagnosis-related group (DRG) data. The costs were in Euros (EUR) or UK pounds sterling and were presented in EUR for all countries. The price year was 2007 to 2008.

Analysis of uncertainty:
A deterministic sensitivity analysis was undertaken on the model inputs, using extreme ranges of values. A multivariate, probabilistic sensitivity analysis was carried out, using probability distributions for the model inputs and cost-effectiveness acceptability curves were generated.

Results
Compared with placebo, zoledronic acid led to a gain of 0.02 QALYs and a reduction of 0.79 skeletal events per patient. It had an extra cost of EUR 17 in France and EUR 178 in the Netherlands, while it saved EUR 288 in Germany, EUR 209 in the UK, and EUR 113 in Portugal.

The incremental cost per QALY gained with zoledronic acid over placebo was EUR 786 in France and EUR 8,278 in the Netherlands. Zoledronic acid was dominant, as it was more effective and less expensive, in Germany, the UK, and Portugal.

In all sensitivity analyses, the incremental cost-utility ratio was below the threshold of EUR 50,000 per QALY. The most influential inputs were the assumptions for overall survival, the number of infusions, and the costs of skeletal events.

Depending on the country, zoledronic acid was cost-saving in 45% to 61% of simulations, and was cost-effective at a threshold of EUR 50,000 per QALY in 65% to 83% of simulations; some uncertainty remained.

Authors' conclusions
The authors concluded that zoledronic acid was cost-saving or cost-effective, compared with placebo, in France, Germany, the UK, Portugal, and the Netherlands.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as zoledronic acid was the only bisphosphonate that was proven to safely and effectively reduce skeletal events in patients with NSCLC.

Effectiveness/benefits:
The clinical data were from a RCT that should have had high internal validity and was partly described, with its reference (Rosen, et al 2003, see 'Other Publications of Related Interest' below for bibliographic details). In this trial, overall survival was higher for zoledronic acid, but the difference was not statistically significant and survival was assumed to be the same for both options, as a conservative estimate against zoledronic acid. The authors did not state if other clinical trials of zoledronic acid were available for the analysis. Most of the clinical inputs were varied in the sensitivity analysis. QALYs were an appropriate measure of benefit as they take account of the impact of NSCLC on life expectancy and quality of life, and they allow comparisons with other disease treatments. The utility weights were assessed using a valid and recommended instrument and were appropriate. The duration of disutility due to skeletal events was uncertain.

Costs:
The cost categories were consistent with the authors' stated perspective. A breakdown of cost items was provided for some categories, with the quantities of resources and the unit costs in an appendix, while other categories were reported as totals. The authors acknowledged that DRG data might overestimate the true health care costs, as out-patient cases were presumed to be less expensive and were ignored. Reflation exercises will be possible as the price year was reported. Variations in economic data were considered in the sensitivity analyses.

Analysis and results:
The results were extensively presented for each country. An appropriate incremental approach used to combine the costs and benefits of the two treatments. Valid approaches were used to examine the uncertainty and the findings were
clearly illustrated. Discounting was not required given the poor survival of these patients. The analysis was conducted in several countries and the results might be transferable to other countries with similar cost structures, such as most European countries. The authors acknowledged some assumptions that might have biased the results in favour of or against zoledronic acid. In general, these issues were investigated in the extensive sensitivity analysis.

Concluding remarks:
: The cost-effectiveness methods were appropriate, which should make the authors’ conclusions valid.

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