Cost-effectiveness of pemetrexed plus cisplatin: malignant pleural mesothelioma treatment in UK clinical practice

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 assess the cost-effectiveness of pemetrexed plus cisplatin versus cisplatin and alternative treatments for malignant pleural mesothelioma. The authors concluded that pemetrexed plus cisplatin demonstrated acceptable cost-effectiveness compared with the alternatives. The methodology was appropriate, but although the results were reported in detail, the methods used were not. The authors’ conclusions do not reflect the results, which reported incremental cost-utility ratios of over £40,000 per QALY for pemetrexed plus cisplatin when compared with cisplatin.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of pemetrexed plus cisplatin versus cisplatin monotherapy, and other alternatives, in the treatment of malignant pleural mesothelioma.

Interventions
The study assessed the use of pemetrexed plus cisplatin therapy. This intervention was compared with cisplatin monotherapy; mitomycin-C, vinblastine and cisplatin (MVP); vinorelbine; and active symptom control.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The authors reported that two trial-based models were developed to assess the costs and outcomes of each of the interventions. The first model compared the cost-effectiveness of pemetrexed plus cisplatin versus cisplatin monotherapy (model one). The second model compared the cost-effectiveness of pemetrexed plus cisplatin versus MVP (mitomycin-C, vinblastine plus cisplatin), vinorelbine and active symptom control (model two). The time horizon of the analysis was 29 months. The authors reported that the perspective adopted in the economic analysis was that of the UK National Health Service (NHS).

Effectiveness data:
The effectiveness and clinical data used in model one were derived from a phase III randomised clinical trial (i.e. EMPHACIS trial). The authors reported that the trial consisted of 448 patients all analysed on an intention to treat basis. The main outcome of the trial was survival. No further details of the trial were reported. Outcomes of the pemetrexed plus cisplatin arm of model two were derived from the EMPHACIS trial. For the other three interventions studied in the model, duration of treatment, likely adverse event rates, survival outcomes and symptom control were derived from a systematic review of the clinical literature.

Monetary benefit and utility valuations:
In model one, utility estimates were derived from the ACTION study (Bischoff, et al. 2005 see ‘Other Publications of Related Interest’ below for bibliographic details). In model two, utility estimates were derived from the ACTION study and other studies identified in a review of the literature.
Measure of benefit:
The measures of benefit were life-years and quality-adjusted life-years (QALYs) gained.

Cost data:
The direct costs included in the analysis were those relating to: study treatments; chemotherapy administration both as an out-patient and an in-patient; vitamin B and folic acid treatment; post-study chemotherapy; and adverse event hospitalisations. In model one, and in the pemetrexed plus cisplatin arm of model two, resource use was derived from the EMPHACIS trial. The remaining resource use information for model two was derived from a literature review, supplemented by market research survey results. Unit costs were derived from NHS reference costs, a compendium of statistics on health and social care and drug price lists. Although discounting of future costs took place, the authors did not report the annual rate used. The price year was not explicitly reported. All costs were reported in UK pounds sterling (£).

Analysis of uncertainty:
The robustness of the cost-effectiveness models was tested using one-way sensitivity analyses. Those variables exerting the greatest influence on cost-effectiveness were included in a subsequent two-way sensitivity analysis. In addition, for model one, the authors assessed the cost-effectiveness of pemetrexed plus cisplatin versus cisplatin alone by comparing different subgroups: all patients; patients with advanced disease; patients with performance score 0 or 1; and those patients with advanced disease and performance score 0 or 1.

Results
Model one

The discounted average survival gain in patients treated with pemetrexed plus cisplatin ranged from 0.20 to 0.28 life-years compared with cisplatin monotherapy. In terms of QALYs gained, pemetrexed plus cisplatin was associated with gains ranging from 0.13 to 0.20. The associated average incremental costs associated with pemetrexed plus cisplatin treatment ranged from £8,779 to £9,020 compared with cisplatin monotherapy.

The average incremental cost per life-year gained when pemetrexed plus cisplatin was compared with cisplatin monotherapy ranged from £31,337 in patients with advanced disease and performance score 0 or 1 to £44,264 for all patients.

The average incremental cost per QALY gained when pemetrexed plus cisplatin was compared with cisplatin monotherapy ranged from £44,950 in patients with advanced disease and performance score 0 or 1 to £68,599 for all patients.

Model two

Pemetrexed plus cisplatin was associated with increases of 0.521 life-years compared with MVP (mitomycin-C, vinblastine plus cisplatin), 0.218 life-years compared with vinorelbine, and 0.530 life-years compared with active symptom control. Pemetrexed plus cisplatin was associated with increases of 0.350 QALYs compared with MVP, 0.142 QALYs compared with vinorelbine, and 0.356 QALYs compared with active symptom control. Pemetrexed plus cisplatin was associated with incremental costs of £7,604 compared with MVP, £3,748 compared with vinorelbine, and £11,410 compared with active symptom control.

The average incremental cost per life-year gained for pemetrexed plus cisplatin was £14,595 when compared with MVP, £17,156 when compared with vinorelbine, and £21,545 when compared with active symptom control.

The average incremental cost per QALY gained for pemetrexed plus cisplatin was £21,731 when compared with MVP, £26,437 when compared with vinorelbine and £32,066 when compared with active symptom control.

Authors’ conclusions
The authors reported that pemetrexed plus cisplatin demonstrated acceptable cost-effectiveness when compared with cisplatin monotherapy and alternative treatments commonly used in clinical practice.
CRD commentary

Interventions:
All the interventions were well reported. In addition, a justification was given for the comparators used, namely that they represented current practice in the UK.

Effectiveness/benefits:
The authors reported that the effectiveness data used in model one, and part of model two, were derived from a phase-III randomised controlled trial (RCT) including 448 patients. Although few details of the trial were reported, it would appear that the use of this trial to derive effectiveness data was appropriate given the fact that RCTs are considered to be the gold-standard method for comparing the effectiveness of health interventions. For model two, in addition to data from the trial, effectiveness data were derived from a systematic review of the literature, no details of which were reported. As a result, it was unclear if all relevant data were included. The sources of utility data, from which QALYs were generated, were appropriately reported and appear to be valid.

Costs:
The perspective adopted in the study was adequately reported. Given this perspective, it appeared that no relevant categories of cost or resource use were omitted from the analysis. The sources of resource use and unit cost data were appropriately reported. However, the authors did not report the discount rate used or the price year.

Analysis and results:
Only a few details of the models used were reported, with no diagrams. Uncertainty in the model was assessed using a series of one-way and two-way sensitivity analyses, the results of which were reported in full. However, the use of probabilistic sensitivity analyses to assess the overall uncertainty in a model is considered to be the gold standard in the UK. As the only limitation to their study, the authors reported the absence of phase-III clinical trials for other alternative regimens. This meant that the quality of evidence was compromised when compared with direct trial-based comparisons of cisplatin.

Concluding remarks:
The quality of the study methodology was appropriate. Although the results of the model were reported in full detail, the methods used were not. Also, the authors’ conclusion that pemetrexed plus cisplatin was cost-effective does not seem to follow from the results, which found incremental cost-utility ratios in excess of £40,000 per QALY when compared with cisplatin monotherapy.

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