Cost-effectiveness of pemetrexed plus cisplatin as first-line therapy for advanced nonsquamous non-small cell lung cancer

Klein R, Muehlenbein C, Liepa AM, Babineaux S, Wielage R, Schwartzberg L

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 aim was to evaluate the cost-effectiveness of first-line cisplatin and pemetrexed, compared with cisplatin and gemcitabine, for patients with advanced non-squamous non-small cell lung cancer (NSCLC) and all patients with advanced NSCLC. Cisplatin plus pemetrexed might be considered to be cost-effective, particularly for patients with advanced non-squamous NSCLC. The poor reporting of the identification and synthesis of the model inputs makes it difficult to assess their validity and this should be borne in mind when considering the conclusions.

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

Study objective
The aim was to evaluate the cost-effectiveness of treatment combinations as first-line therapy for patients with advanced non-small cell lung cancer (NSCLC), with non-squamous cell histology, and for all patients with advanced NSCLC.

Interventions
The intervention was three-week cycles of cisplatin 75mg per m$^2$ and pemetrexed 500mg per m$^2$ once per cycle, for chemotherapy naive patients with NSCLC. The main comparator was cisplatin 75mg per m$^2$ once per cycle and gemcitabine 1,250mg per m$^2$ twice per cycle. The other two comparators were carboplatin 100mg per target area under the concentration versus time curve (AUC; assumed to be 6mg per mL minute) and paclitaxel 200mg per m$^2$ once per cycle; and carboplatin 100mg per AUC, paclitaxel 200mg per m$^2$, and bevacizumab 15mg per kg once per cycle.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The study used a semi-Markov state-transition model to combine the data from a head-to-head trial of cisplatin plus pemetrexed versus cisplatin plus gemcitabine, and an indirect mixed-treatment comparison model of cisplatin plus pemetrexed, carboplatin plus paclitaxel, and carboplatin plus paclitaxel plus bevacizumab. The time horizon was two years from initiation of first-line therapy. The authors stated that the perspective was that of the payer.

Effectiveness data:
The effectiveness data came from the combination of the head-to-head phase III clinical trial and the indirect mixed-treatment comparison model. The main clinical effectiveness estimates were the treatment response and the progression and survival rates.

Monetary benefit and utility valuations:
The utility estimates were from a published algorithm, developed for advanced NSCLC, that incorporated toxicity and progression.

Measure of benefit:
The primary measure of benefit was quality-adjusted life-years (QALYs) gained. The authors also reported life-years
Cost data:
The direct health costs included medications and premedications, monitoring, adverse events, subsequent treatment, disease-related morbidity, and palliative care. The cost data were from Medicare reimbursement rates and PharMetrics claims databases. All costs were in US dollars ($).

Analysis of uncertainty:
One-way sensitivity analyses were performed, focusing mainly on the cost inputs and the comparison between cisplatin plus pemetrexed and cisplatin plus gemcitabine. The results were presented in tornado diagrams.

Results
In patients with advanced non-squamous non-small cell lung cancer, the analysis suggested that two-year treatment with carboplatin plus paclitaxel cost $52,885 and yielded 0.8945 life-years and 0.4513 QALYs; cisplatin plus gemcitabine cost $61,008 and yielded 0.9112 life-years and 0.4676 QALYs; cisplatin plus pemetrexed cost $65,517 and yielded 0.9652 life-years and 0.5016 QALYs; and carboplatin, paclitaxel and bevacizumab cost $90,044 and yielded 1.0379 life-years and 0.5260 QALYs.

The cost-utility ratio for cisplatin plus pemetrexed compared with cisplatin plus gemcitabine was $132,829 per QALY gained; for cisplatin plus pemetrexed compared with carboplatin plus paclitaxel the ratio was $250,992 per QALY gained; and the ratio for carboplatin, paclitaxel and bevacizumab compared with cisplatin plus pemetrexed was $1,006,065.

For all patients with NSCLC, carboplatin, paclitaxel and bevacizumab was not considered. The cost-utility ratio for cisplatin plus pemetrexed compared with cisplatin plus gemcitabine was $175,597 per QALY gained; and for cisplatin plus pemetrexed compared with carboplatin plus paclitaxel it was $343,870 per QALY gained.

The results of the univariate sensitivity analyses suggested that reasonable changes in the costs changed the cost-utility ratio for cisplatin plus pemetrexed compared with cisplatin plus gemcitabine by less than 10%.

Authors’ conclusions
The authors concluded that cisplatin plus pemetrexed might be considered to be cost-effective, particularly for patients with advanced non-squamous NSCLC.

CRD commentary
Interventions:
The interventions were well described. The analysis included the commonly used and widely reimbursed first-line chemotherapy regimens in the authors setting and therefore should reflect the usual practice.

Effectiveness/benefits:
The effectiveness data were primarily from two sources, one of which was a head-to-head randomised controlled trial and the other was a network analysis that allowed the relative estimates of effectiveness to be derived despite of a lack of head-to-head trials. The authors did not provide any information or detail on the head-to-head trial, nor on the trials included in the network analysis. No details of the identification, selection, and synthesis of the data were presented. This makes it impossible to determine the validity of the clinical evidence and whether the best data were used. The utilities were from a published study and the value for each model health state was given, but no other details were reported. QALYs were an appropriate outcome to capture the impact of disease on quality of life and survival, but without these details it is not possible to ascertain the validity of the estimates used.

Costs:
The perspective was clearly defined and it appears that all relevant costs were considered. The disease costs were presented as category totals and the resource use was not provided, which limits the generalisability and makes it impossible to assess how robust or appropriate the resource use estimates were. The price year was not provided. No discounting was applied in view of the short (two-year) time horizon.
Analysis and results:
The authors did not undertake a full incremental analysis; instead they presented each comparator compared with cisplatin plus pemetrexed. The model was well described and a diagram provided. The assumptions required to facilitate the analysis were clearly presented. The uncertainty was assessed, using one-way sensitivity analyses, but a probabilistic sensitivity analysis would have allowed a more comprehensive assessment of the overall impact of parameter uncertainty. There appears to have been little evidence available, which means that there was likely to be high uncertainty and this should have been fully assessed. The results of the base case, secondary analysis, and sensitivity analyses were satisfactorily reported. The authors discussed and acknowledged a number of limitations to their study.

Concluding remarks:
The poor reporting of the identification and synthesis of the model inputs makes it difficult to assess their validity and this should be borne in mind when considering the conclusions.

Funding
Funding received from Eli Lilly and Company.

Bibliographic details

PubMedID
19786904

DOI
10.1097/JTO.0b013e3181ba31e0

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Agents /economics /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy /economics /pathology; Cisplatin /economics /therapeutic use; Cost-Benefit Analysis; Drosophila Proteins; Drug Costs; Drug Therapy, Combination; Endopeptidases; Female; Follow-Up Studies; Glutamates /economics /therapeutic use; Guanine /analogs & derivatives /economics /therapeutic use; Humans; Lung Neoplasms /drug therapy /economics /pathology; Male; Middle Aged; Models, Economic; Neoplasm Staging; Pemetrexed; Retrospective Studies; Thymidylate Synthase /antagonists & inhibitors; United States

AccessionNumber
22010000060

Date bibliographic record published
04/08/2010

Date abstract record published
27/07/2011