Raltitrexed plus cisplatin is cost-effective compared with pemetrexed plus cisplatin in patients with malignant pleural mesothelioma

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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 assessed the cost-effectiveness of raltitrexed plus cisplatin compared with pemetrexed plus cisplatin treatment for patients with malignant pleural mesothelioma (lung cancer). The authors concluded that raltitrexed plus cisplatin was a cost-effective first-line treatment. The quality of the study was adequate with methods and results reported in detail. Although the authors' conclusions are appropriate, it should be noted that the results presented are subject to some uncertainty.

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

Study objective
The objective was to assess the cost-effectiveness of raltitrexed plus cisplatin compared with pemetrexed plus cisplatin in patients with malignant pleural mesothelioma (a form of lung cancer).

Interventions
Four treatments for malignant pleural mesothelioma were compared: active symptom control; cisplatin monotherapy; raltitrexed plus cisplatin; and pemetrexed plus cisplatin.

Location/setting
UK/In-patient secondary care.

Methods
Analytical approach:
A partitioned survival approach was used to model lifetime costs and health outcomes associated with each treatment pathway. The time horizon was five years, which was the lifetime time horizon for this patient population. The authors reported that the UK NHS and personal social services perspective was adopted.

Effectiveness data:
Clinical and effectiveness information came from published studies. A review of the literature was undertaken to supplement the findings of a previous systematic review (Ellis, et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). The authors searched EMBASE, MEDLINE and The Cochrane Library from January 2005 to June 2010; only randomised controlled trials (RCTs) published in English were included in the study. The main effectiveness estimates used in the model were the hazard ratios for progression free and overall survival. With the exception of the comparison between cisplatin and active symptom control (which the authors assumed to have a hazard ratio of 1), the effectiveness estimates were derived from trials identified through the review. Indirect comparisons had to be made as not all interventions were compared head-to-head.

Monetary benefit and utility valuations:
The utility estimates were taken from a number of trials and studies that evaluated the quality of life in patients with lung cancer.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were the summary measures of benefit. These were discounted...
using an annual rate of 3.5%.

Cost data:
The direct costs included: chemotherapy treatments and administration; follow-up including CT scans and clinical evaluations; treatment of adverse events including anaemia, constipation, fatigue, infection and phlebitis; and use of concomitant medications. Treatment regimens were obtained from the published trials and valued using costs published in the British National Formulary. Costs of chemotherapy administration and follow-up came from NHS reference costs. Adverse event rates were from published trials, with each event costed using National Institute for Health and Clinical Excellence (NICE) appraisals and treatment algorithms informed by clinical opinion. All costs were reported in UK £. The price year was 2009. Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken. In addition, a probabilistic sensitivity analysis was carried out to assess the impact of the joint uncertainty in all parameter values on the model results. For this analysis, all model parameters were fitted with probability distributions, with a series of Monte Carlo simulations being undertaken; the results were presented as cost-effectiveness acceptability curves.

Results
For active symptom control of malignant pleural mesothelioma, life-years were 1.08, QALYs were 0.68 and the cost per patient was £1,358.

For cisplatin monotherapy, life-years were 1.08, QALYs were 0.68 and the cost per patient was £4,288.

For raltitrexed plus cisplatin, life-years were 1.37, QALYs were 0.89 and the cost per patient was £7,122.

For pemetrexed plus cisplatin, life-years were 1.36, QALYs were 0.88 and the cost per patient was £12,064.

Costs and benefits were combined using an incremental cost-effectiveness ratio (ICER, the additional cost per life-year gained) and an incremental cost-utility ratio (ICUR, the additional cost per QALY gained). Cisplatin dominated active symptom control (which was more costly and less effective). When compared with active symptom control, the ICER for raltitrexed plus cisplatin was £19,340 per life year gained and the ICUR was £27,360 per QALY gained. Raltitrexed plus cisplatin dominated pemetrexed plus cisplatin as it had slightly higher QALYs and life years at a much lower total cost.

Results of the probabilistic sensitivity analysis showed that, at a willingness to pay threshold of £20,000 to £30,000 per QALY gained, raltitrexed plus cisplatin was the intervention most likely to be cost-effective, with a probability that ranged from 31% to 52%.

Authors’ conclusions
The authors concluded that raltitrexed plus cisplatin was a cost-effective first-line treatment for malignant pleural mesothelioma.

CRD commentary
Interventions:
The interventions under study were reported adequately. The rationale for the selection of the comparators was appropriate as they represented available treatments in the authors setting.

Effectiveness/benefits:
Clinical and effectiveness evidence were mainly taken from a previous systematic review, which was updated by the authors. Adequate details of the literature search were reported including key terms used, inclusion and exclusion criteria and the databases searched. Although the authors did not report whether the search was systematic in nature, it was likely that all major relevant published evidence was identified. Most of the data came from published RCTs which were likely to be of high quality. The method used to combine clinical data appeared to have been appropriate and was adequately described. QALYs and life-years were appropriate benefit measures to capture the impact of the disease on patients’ health and allowed comparisons with the benefits of other health care interventions. The sources of utility data
(for QALYs) were reported and appeared to be valid.

Costs:
The authors explicitly reported that a NHS and social services perspective was adopted; all major relevant costs appear to have been included. Unit costs and resource use quantities were generally presented separately, which enhanced the transparency of the analysis. The sources used were adequately reported. The price year, time horizon, discount rate used and currency details were all reported.

Analysis and results:
The authors used a partitioned survival approach to model lifetime costs and health outcomes for each intervention. The authors reported that this approach was commonly used for studies that evaluated late stage cancer interventions. Appropriate details of the methods used were reported. Uncertainty in the model was adequately evaluated using one-way sensitivity analyses and probabilistic sensitivity analysis; the methods were described. The main results were presented clearly and discussed. The incremental approach used to synthesise costs and benefits of the alternative strategies was appropriate. The authors acknowledged that a main limitation to their study was that for their adjusted indirect comparisons to be valid, the different clinical trials used should have had no differences that could modify relative treatment effects. The authors also reported some differences in histology composition and performance status between trials, which introduced uncertainty.

Concluding remarks:
Overall the quality of the study was adequate with methods and results reported in detail. Although the authors’ conclusions are appropriate, the results presented are subject to some uncertainty.

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