An economic analysis of erlotinib, docetaxel, pemetrexed and best supportive care as second or third line treatment of non-small cell lung cancer


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 evaluated the costs and benefits of erlotinib as second- or third-line treatment for advanced or metastatic non-small cell lung cancer, compared with docetaxel, pemetrexed, and best supportive care. The authors concluded that erlotinib instead of docetaxel or pemetrexed could produce annual savings for the Portuguese National Health Service, with a gain in quality-adjusted life-years. There were significant limitations to the study design and reporting and the authors' conclusions should be considered with caution.

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

Study objective
The aim was to evaluate costs and benefits of erlotinib as second- or third-line treatment for advanced or metastatic non-small cell lung cancer in patients who had failed to respond to at least one prior chemotherapy regimen.

Interventions
The interventions were erlotinib 150mg per day (four cycles of seven days a month), docetaxel 75mg per m\(^2\) (on the first day of 21-day cycles), and pemetrexed 500mg per m\(^2\) (first day of 21-day cycles), in patients with advanced or metastatic non-small cell lung cancer (stages IIIA, IIIB, or IV), compared with best supportive care.

Location/setting
Portugal/in-patient and out-patient care.

Methods
Analytical approach:
A state-transition model, with a two-year time horizon, was used for progression-free and overall survival curves from clinical trials. The authors stated that a Portuguese National Health Service perspective was used.

Effectiveness data:
The evidence came from three efficacy trials, each of which compared two of the four comparators; treatments were compared indirectly. The authors stated that they used Kaplan-Meier survival curves for the first two years and then a Weibull or log-logistic distribution for an extrapolation to 36 months. The authors assumed that there were no differences among erlotinib, docetaxel or pemetrexed in time spent free from progression or overall survival. No search strategy or inclusion criteria for the review were described.

Monetary benefit and utility valuations:
The utilities for different tumour stages and adverse events were from an unpublished UK study of 154 healthy patients, carried out by Roche, using the European Quality of life (EQ-5D) visual analogue scale.

Measure of benefit:
Life-years gained and quality-adjusted life-years (QALYs) were the measures of benefit. Future benefits were discounted at 5% per annum.

Cost data:
Costs included those for the different health states and adverse events and medications. Resource use was estimated by a Portuguese expert panel of six pneumologists and two oncologists. Unit costs were estimated from several official sources. Costs were reported in Euros (EUR) and the price year was 2008. Older costs were revalued using annual inflation rate data. Future costs were discounted at a rate of 5% per annum.

Analysis of uncertainty:
Different scenario analyses were performed. Subgroups were modelled according to Eastern Cooperative Oncology Group (ECOG) performance status or only second- or third-line chemotherapy. A three-year time horizon was tested using different survival distributional assumptions. Probabilistic sensitivity analysis was performed. Cost-effectiveness scatter plots and percentile confidence intervals were reported.

Results
In the base case, QALYs per patient at two years were 0.250 for erlotinib, 0.186 for supportive care, 0.225 for docetaxel, and 0.241 for pemetrexed. Costs were EUR 26,478 for erlotinib, EUR 16,112 for supportive care, EUR 29,262 for docetaxel, and EUR 32,762 for pemetrexed. The incremental cost-effectiveness ratio (ICER) of erlotinib versus supportive care was EUR 161,742 per QALY. The corresponding incremental cost per life-year gained was EUR 70,424.

Erlotinib dominated docetaxel and pemetrexed as it was more effective and less costly. The results were robust in the sensitivity analyses. Probabilistic sensitivity analyses showed that for most simulations ICER of erlotinib versus supportive care was above the EUR 30,000 per QALY willingness-to-pay threshold for both a life-year gained and a QALY.

Authors' conclusions
The authors concluded that use of erlotinib instead of docetaxel or pemetrexed could contribute to annual savings for the Portuguese NHS with a gain in QALYs. They also stated that these results should be confirmed by randomised parallel clinical trials comparing the treatments directly.

CRD commentary
Interventions:
The interventions were adequately described and standard care was appropriately included. The reader should decide if these comparators are relevant in their own setting.

Effectiveness/benefits:
The authors did not state whether the trials included were the only relevant trials available. They acknowledged the assumption that these three trials were comparable. They could have included survival curves for each comparator and included distributions for the extrapolation or modelled survival curves for the entire time periods of each state and included distributions for those. They also reported the limitation that UK utilities from unpublished data were used for the Portuguese population.

Costs:
Relevant cost categories were included for the selected perspective. Resource use was derived from expert opinion and the methods were not described in detail. Other aspects of the costing were reported adequately.

Analysis and results:
The authors reported a cost-minimisation analysis as well as cost-effectiveness and cost-utility analyses, but not all the comparators had equal effectiveness. The cost-effectiveness and cost-utility analyses were more relevant. The data appear to have been reported selectively to favour erlotinib treatment. For example, the ICER of erlotinib versus supportive care was EUR 161,742 per QALY and in most simulations the ICER was above the EUR 30,000 per QALY willingness-to-pay threshold, but this was not reported to mean that erlotinib was not cost-effective compared with supportive care.

Concluding remarks:
Significant limitations to the study design and reporting mean that the authors’ conclusions should be considered with caution.

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