Cost-effectiveness of erlotinib versus docetaxel for second-line treatment of advanced non-small-cell lung cancer in the United Kingdom

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Record Status
This is a critical structured 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 erlotinib compared with docetaxel in the second-line management of advanced non-small cell lung cancer (NSCLC). The authors concluded that erlotinib was more effective and less expensive from the perspective of the UK NHS for the treatment of relapsed patients with stage III to IV NSCLC. Although the study appears to have been well performed and various sensitivity analyses were undertaken, a significant amount of uncertainty remains. The results should be considered with this uncertainty in mind.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of erlotinib compared with docetaxel in the second-line management of advanced non-small cell lung cancer (NSCLC).

Interventions
Erlotinib (150mg per m\(^2\) per day) was compared with docetaxel (75mg per m\(^2\) per day).

Location/setting
UK/secondary care.

Methods
Analytical approach:
The analysis was based on a state-transition model with a two-year horizon. The authors stated that the perspective of the UK National Health Service (NHS) was adopted.

Effectiveness data:
The clinical data were mostly from two randomised controlled trials (RCTs); BR.21, with 731 patients receiving erlotinib or placebo, and TAX 317, with 155 patients receiving docetaxel or best supportive care. There were no head-to-head trials and some assumptions were made, such as that the overall survival for both drugs was equivalent. The key clinical inputs were the rate and type of adverse events with the two drugs.

Monetary benefit and utility valuations:
The utility values were derived, using a visual analogue scale (VAS), with a sample of 154 members of the general population from four UK sites.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the benefit measure and those accrued in the second year were discounted at a rate of 3.5%.

Cost data:
The economic analysis included the costs of drug acquisition and administration, disease progression, and treatment of adverse events. These costs were from NHS Reference Costs and from the Personal Social Services Research Unit.
Hospital and Community Health Services. The data on resource consumption for all health states and adverse events were from the expert opinion of a panel of five UK lung cancer physicians. The data on drug dosages were from the two trials that supplied the clinical efficacy and safety data. All costs were in UK pounds sterling (£) and those incurred over the second year were discounted at a rate of 3.5%.

Analysis of uncertainty:
A deterministic univariate analysis was undertaken on the following inputs: the cost of managing febrile neutropenia, cost of docetaxel administration, cost of the progression-free health state, cost of progressive disease, utility scores for both progression-free survival and progression, and the rate of febrile neutropenia. Plausible ranges of values were used. Alternative scenarios were analysed, with equivalent overall survival and disease-free survival, equivalent utility scores for progression-free survival, equivalent treatment durations, and the omission of adverse event utilities from the model. A probabilistic analysis, based on a Monte Carlo simulation, was also carried out.

Results
In the base case, erlotinib led to a saving of £226 and a gain of 0.032 QALYs compared with docetaxel, which meant that erlotinib was dominant (cheaper and more effective). The greatest savings were achieved in adverse event costs and administration costs, which were far lower for erlotinib patients.

The sensitivity analysis showed that the results were robust, except when docetaxel administration costs were reduced, the cost of the progression health state was reduced, or the utility score for progression-free survival for docetaxel was increased.

The probabilistic analysis showed that erlotinib remained cost-effective at a threshold of £30,000 per QALY in 70% of simulations, and was cost-saving in 36%.

Authors’ conclusions
The authors concluded that erlotinib was more effective and less expensive than docetaxel, from the perspective of the UK NHS, for the treatment of relapsed stage III to IV NSCLC patients.

CRD commentary
Interventions:
The rationale for the selection of the comparators was explicitly stated and both therapies were recommended by the UK National Institute for Health and Clinical Excellence (NICE), for the second-line treatment of advanced NSCLC.

Effectiveness/benefits:
The clinical data were from a selection of relevant studies, but no systematic review was reported and relevant data might have been missed. Most of the data were from two RCTs, which are generally considered to be valid sources of evidence due to their robust methods. There were no published head-to-head clinical trials of the two drugs and indirect comparison had to be carried out. The authors stated that this comparison might have biased the results in favour of docetaxel, since the patients’ conditions were slightly less severe in the TAX 317 trial. QALYS were an appropriate benefit measure, given the impact of the disease on both quality of life and survival. The authors pointed out that the VAS might not have been the most appropriate instrument to elicit preferences for health conditions, but it was chosen for its simplicity and user friendliness.

Costs:
The categories of costs and their sources were consistent with the viewpoint of the NHS. The unit costs and quantities of resources used were presented separately for most items, increasing the transparency of the analysis. A unique price year was not reported and the costs were from sources published between 2004 and 2008. Alternative cost assumptions were made in the sensitivity analysis.

Analysis and results:
The incremental analysis used to combine the costs and benefits was appropriate. The issue of uncertainty was satisfactorily investigated, using various approaches, but it was not clear whether a first- or second-order Monte Carlo simulation was conducted. The results were clearly presented and discussed. The recommended discounting was
performed for both costs and benefits. In general, the authors stated that model assumptions favoured docetaxel.

**Concluding remarks:**
Although the study appears to have been well performed and various sensitivity analyses were undertaken, a significant amount of uncertainty remains. The results should be considered with this uncertainty in mind.

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