Addition of cetuximab to first-line chemotherapy in patients with advanced non-small-cell lung cancer: a cost-utility analysis


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 examined the cost-effectiveness of adding cetuximab to first-line standard chemotherapy for patients with epidermal growth factor receptor over-expressing, advanced, inoperable, wet stage IIIB or stage IV, non-small cell lung cancer, from the perspective of the Swiss health care system. The authors concluded that adding cetuximab to standard chemotherapy was not cost-effective. Treatment schedules based on intermittent dosing should be evaluated in future studies. The cost-effectiveness framework was valid and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of adding cetuximab to first-line standard chemotherapy for patients with epidermal growth factor receptor over-expressing, advanced, inoperable, wet stage IIIB or stage IV, non-small cell lung cancer (NSCLC).

Interventions
The intervention was cetuximab added to the standard cisplatin-vinorelbine first-line chemotherapy, which was the comparator. Cetuximab was given at a loading dose of 400mg per m$^2$ intravenously over two hours on day one, followed by weekly infusions at a dose of 250mg per m$^2$. Treatment continued until the disease progressed or toxicity became unacceptable.

Location/setting
Switzerland/out-patient setting.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that it was carried out from the perspective of the health care system.

Effectiveness data:
The clinical data were from a published phase III, open-label, randomised controlled trial (RCT); the First-Line EribitiX in lung cancer (FLEX) trial (Pirker, et al. 2009, see ‘Other Publications or Related Interest’ below for bibliographic details). This trial compared cisplatin-vinorelbine first-line chemotherapy with or without cetuximab in the target patient population. It provided data on the time to treatment failure and overall survival, which were the key inputs for the model. Toxicity rates were also from this trial.

Monetary benefit and utility valuations:
The utility values were from a published study.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of medications and chemotherapy, treatment of major adverse events, laboratory tests, and follow-up treatment for progressive disease. The following items were considered: cetuximab, cisplatin, vinorelbine, docetaxel, pemetrexed, erlotinib, preparation and administration of chemotherapy, blood count, computed tomography, hospitalisation, treatment for febrile neutropenia, and radiotherapy. The resource use data were from the RCT. The costs were from official Swiss sources, such as national tariffs and Swiss public prices, and a Swiss lung cancer study. They were assessed in Swiss francs (CHF) and presented in Euros (EUR). The price year was 2009.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on the model inputs, such as overall survival, the utility parameters, number of days in hospital, proportion of patients receiving computed tomography, and proportion of patients with febrile neutropenia. A probabilistic analysis was performed, using a Monte Carlo simulation. The ranges of values and the probability distributions were either from published sources or based on authors’ opinions. Alternative scenarios were analysed with different body surface areas (BSAs) and intermittent cetuximab dosing schedules.

Results
In the base case (with a BSA of 1.77m$^2$), the projected costs were EUR 23,917 with chemotherapy and EUR 50,004 with cetuximab. The QALYs were 0.547 with chemotherapy and 0.617 with cetuximab. The incremental cost per QALY gained with cetuximab over chemotherapy was EUR 376,205. This figure ranged from EUR 308,384 with a BSA of 1.45m$^2$ to EUR 490,651 with a BSA of 2.31m$^2$. All of which were far above the cost-effectiveness threshold of EUR 60,000 per QALY.

The two most influential inputs were the hazard ratios for the time from treatment to failure to death, and for the time to treatment failure, but in no scenario did the incremental cost per QALY gained approach the cost-effectiveness threshold. The probability of cetuximab being cost-effective was effectively zero.

Interritent cetuximab dosing, without varying its efficacy, had a big impact. For example, three cycles of cetuximab, with a total dose of 900mg per m$^2$ per cycle, resulted in an incremental cost per QALY of EUR 83,100, while two cycles with a total dose of 900mg per m$^2$ per cycle, resulted in an incremental cost per QALY of EUR 62,500.

Authors' conclusions
The authors concluded that adding cetuximab to standard chemotherapy was not cost-effective. Treatment schedules based on intermittent dosing should be evaluated in future studies.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the treatment was added to the standard care for patients with advanced NSCLC. The dosages were reported and alternative intermittent dosing was analysed. Cetuximab was not approved by the European Medical Agency for this category of patients.

Effectiveness/benefits:
A published trial was the source for the clinical evidence. This trial was appropriately selected as it was the most recent head-to-head trial comparing the efficacy and safety of the two treatments. Its methods and other characteristics were not reported, but RCTs are generally considered to be valid sources, due to their rigorous design. Little information on the approach used to derive the utility values was provided, but the authors considered wide variations in these inputs in the sensitivity analyses. QALYs were an appropriate benefit measure, because of the impact of the disease on both survival and quality of life for NSCLC patients.

Costs:
The cost categories and their sources were consistent with the perspective. Extensive details of the unit costs and resource quantities were reported, enhancing the transparency of the economic analysis and improving its external validity. Alternative assumptions for the costs and drug dosages were assessed in the sensitivity analyses. The price year and currency conversions were explicitly reported. The resource use data were from clinical trials, which are likely to have provided very detailed estimates, but might not be an accurate reflection of real clinical patterns.
Analysis and results:
The results were clearly presented. An incremental approach was used to synthesise the costs and benefits of the two treatments. Alternative scenarios were analysed in the sensitivity analyses. The uncertainty appears to have been satisfactorily investigated. The authors pointed out that discounting was not relevant because of the poor survival of this patient population. The model was validated using data from the FLEX trial. The authors compared their results with those of other published economic evaluations that generally came to the same conclusions. The analysis appears to be transferable to settings with a similar cost structure.

Concluding remarks:
The cost-effectiveness framework was valid and the authors’ conclusions appear to be robust.

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