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 epidermal growth factor receptor (EGFR) testing and first-line treatment with gefitinib in advanced lung adenocarcinoma patients with EGFR activating mutations. The authors concluded that this combination was more effective and less costly than treating the whole population with first-line chemotherapy without testing. The results obtained are uncertain and a lack of detailed reporting inhibits a full critique. The conclusions presented cannot be considered robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of epidermal growth factor receptor (EGFR) testing and first-line treatment with gefitinib in advanced lung adenocarcinoma patients with EGFR activating mutations.

Interventions
The intervention was EGFR mutation testing followed by first-line treatment with gefitinib for patients with activating EGFR mutations (positive testing results) and if necessary second-line chemotherapy; and first-line treatment with chemotherapy followed if necessary by best supportive care for those with negative testing results. The comparator was standard care that included first-line treatment with chemotherapy and second-line treatment with gefitinib.

Location/setting
Singapore/Secondary care

Methods
Analytical approach:
A decision tree model was used to synthesise data and compare the interventions and outcomes. The authors reported that a payer’s perspective was adopted.

Effectiveness data:
The primary effectiveness data was overall survival derived by pooling data from three trials of gefitinib compared to chemotherapy regimens. The EGFR mutation test was assumed to achieve a positive test rate of 60% based on data from the IPASS trial (see Other Publications of Related Interest). Patients progressed through lines of treatment according to estimates of time receiving each treatment line based on data from the three trials according to EGFR status. Time in first-line treatment was based on median progression-free survival. Overall survival was assumed to be the same regardless of which first-line treatment was received.

Monetary benefit and utility valuations:
Baseline utility values and utility decrements for adverse events were derived from a UK health technology assessment of erlotinib for treatment of relapsed non-small cell lung cancer and two other published studies. Values were assigned to states by whether treatment was first line or later, modified by EGFR status.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary measure of benefit.
Cost data:
Direct costs included payments from patients or government payers for chemotherapy with gemcitabine and carboplatin, gefitinib, laboratory tests, physician visits and treatment complications. Costs were a weighted average derived from three cancer centres in Singapore. Cost data were reported in 2010 Singapore dollars (SGD).

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all model inputs, including prevalence of activating EGFR mutations and EGFR mutation testing costs. Additional scenario analyses included added additional chemotherapeutic drugs to treatment, scenarios of gefitinib versus no gefitinib in the EGFR testing strategy and use of gefitinib in patients without mutations.

Results
In the base case, costs and QALYs were SGD 47,100 and 0.87 with standard treatment and SGD 44,700 and 0.91 with EGFR testing and first-line treatment with gefitinib. EGFR testing and first-line treatment with gefitinib dominated standard treatment in that it increased QALYs by 0.04 while reducing costs by SGD 2,400.

The authors found that adding additional chemotherapy agents increased QALYs and costs but did not change overall cost-effectiveness results. Where gefitinib was not given as a second line therapy, the incremental cost-effectiveness ratio (ICER) increased to SGD 77,160 per QALY. Gefitinib was found to be cost-ineffective in patients without an EGFR mutation with an ICER between SGD 129,000 and 196,000 per QALY. First-line treatment with gefitinib was also dominant in the analysis of a subset of patients with activating EGFR mutations.

Authors’ conclusions
The authors concluded that EGFR testing followed by first-line treatment with gefitinib in positive patients was more effective and less costly than treating the whole population with first-line chemotherapy without testing.

CRD commentary
Interventions:
It was not clear why gemcitabine plus carboplatin was chosen as the chemotherapy regimen. None of the trials used to inform effectiveness of chemotherapy had gemcitabine included in the chemotherapeutic agents used in the trial. Effectiveness and costs may vary between different chemotherapy regimens; it was unclear what effect this may have on results.

Effectiveness/benefits:
Overall survival was derived from a pooled analysis of three trials. No pooling methods were reported other than stating that studies were weighted by population size so it was not possible to comment on the level of heterogeneity or the appropriateness of pooling methods. The three trials evaluated gefitinib with different chemotherapy regimens in populations with and without the EGFR mutation. No details were presented on the identification and selection of these trials so it was unclear whether the best available evidence was used. There were some assumptions about time on each treatment and overall survival was not presented in enough detail to allow a critique. This made the results very uncertain.

Assumptions surrounding assignment of utility scores to states appeared appropriate but many aspects of the utility values remained unclear. The method of utility derivation and specific values for utility decrements and symptoms associated with those decrements were not reported. It was not reported how the utility studies were found or selected so it was unclear that the best available utility data was used.

Costs:
Cost categories and their sources were consistent with the stated perspective and setting. Multiple chemotherapy regimens were used to inform effectiveness but only gemcitabine plus carboplatin was used for costs and it was unclear whether this would influence conclusions. Costs were reported in aggregate with little detail so it was unclear how well the costs of this study would transfer to another setting.

Some variation in costs was assessed in the sensitivity analysis. The price year was explicitly reported.
Analysis and results:
The incremental analysis was conducted appropriately and one way and scenario analyses were thorough and appeared well conducted. Some structural uncertainty was analysed, which was appropriate, but parameter uncertainty was not fully addressed. One way sensitivity analyses appeared to indicate a considerable amount of parameter uncertainty that a probabilistic sensitivity analysis would have better explained. The authors analysed adding or exchanging other chemotherapeutic agents as sensitivity analyses but it was unclear how this sensitivity analysis was undertaken.

The authors discussed thoroughly how the results of their studies compared to other studies and it appeared that the underlying prevalence of EGFR mutation was the key factor in whether the testing would be cost-effective.

Concluding remarks:
The results obtained are uncertain and a lack of detailed reporting inhibits a full critique. The conclusions presented cannot be considered robust.

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