Topotecan for relapsed small cell lung cancer: a systematic review and economic evaluation

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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 clinical effectiveness and cost-effectiveness of topotecan for patients with relapsed small-cell lung cancer. Compared with best supportive care, the addition of oral topotecan was associated with improved health outcomes, but an increased cost. The incremental cost-effectiveness ratio was at the upper end of the range usually seen as cost-effective, from an NHS decision-making perspective. On the whole, the methods seem to have been reasonable and were adequately reported. The authors’ conclusions appear to be appropriate.

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

Study objective
This study assessed the clinical effectiveness and cost-effectiveness of topotecan for patients with relapsed small-cell lung cancer.

Note from the authors: Although oral topotecan vs BSC was the primary focus of the economic evaluation the included studies also looked at oral and IV topotecan, CAV, BSC and amrubicin.

Interventions
Oral topotecan was given as second-line chemotherapy, in addition to best supportive care, and was compared with best supportive care alone.

Location/setting
UK/tertiary care.

Methods
Analytical approach:
A state-transition model, with three states (stable disease, progressive disease, and death), was developed to combine the data from published studies. The time horizon covered the lifetime of the patients. The authors stated that the perspective was that of the UK NHS and Personal Social Services (PSS).

Effectiveness data:
The effectiveness data were from a systematic literature review. Seventeen databases were searched (including the Cochrane Library, MEDLINE, and EMBASE) for articles from 1990 to February 2009, and 10 publications on five randomised controlled trials were selected. The authors used their judgement to select the most appropriate estimates from this evidence, as a meta-analysis was not possible due to heterogeneity between the trials. Parametric survival functions were estimated from Kaplan Meier curves reported in the trials, and were used to estimate the mean time to progression and the overall survival, which were the main clinical effectiveness estimates.

Monetary benefit and utility valuations:
The mean survival estimates were adjusted for quality of life, using health-state European Quality of life (EQ-5D) questionnaire utilities reported in a published study.

Measure of benefit:
The benefits were measured through the gain in life-years and quality-adjusted life-years (QALYs). A discount rate of
3.5% was applied to the benefits over the lifetime of the patients.

Cost data:
The health care costs included pre-medication, drug acquisition, drug administration, patient monitoring, management of adverse events, and palliative care. Several sources were used, including NHS Reference costs and the finance department of Southampton University. All costs were presented in 2007 to 2008 UK pounds sterling (£) and a discount rate of 3.5% was applied.

Analysis of uncertainty:
Parameter uncertainty was assessed in a probabilistic sensitivity analysis. A deterministic sensitivity analysis was carried out to investigate the uncertainty in the model structure, assumptions, and some parameters that were particularly uncertain. A cost-effectiveness acceptability curve was constructed.

Results
The mean cost of best supportive care was £4,854, compared with £11,048 for topotecan plus supportive care. There was a mean gain of 0.2247 QALYs with best supportive care, compared with 0.4077 with topotecan.

Compared with best supportive care, the incremental cost per life-year gained with topotecan was £19,065 and the incremental cost per QALY gained was £33,851.

In the deterministic sensitivity analysis, the results were generally robust. In the probabilistic sensitivity analysis, the topotecan arm was associated with increased QALYs and increased costs in all the simulations, compared with supportive care. The cost-effectiveness acceptability curve showed that topotecan was cost-effective in 20% of simulations at a willingness-to-pay of £30,000 and 100% of simulations at a willingness-to-pay of £50,000 per QALY.

Authors' conclusions
Compared with best supportive care, the addition of oral topotecan was associated with improved health outcomes, but an increased cost. The incremental cost-effectiveness ratio was at the upper end of the range usually regarded as cost-effective from an NHS decision-making perspective.

CRD commentary
Interventions:
The interventions were described and appear to have been appropriate comparators. Justifications were given for not including other relevant comparators.

Effectiveness/benefits:
A systematic review was undertaken to identify the effectiveness data. This should ensure that the best available evidence was used. The search, identification, and selection methods for the included studies were described. The health benefits were appropriately discounted, but little information was given on the methods used to derive the QALYs. The utilities were from a published economic evaluation and this should be consulted to assess their quality.

Costs:
The perspective was explicitly stated and the costs appear to have been appropriate to this perspective. Various sources were used for the costs and a price index was used to inflate some prices. The reporting was good and a table of the unit costs was given.

Analysis and results:
The model structure was described in full and a diagram was presented. The results were clearly reported and appropriately combined in an incremental analysis. The uncertainty around these results was explored well. The authors reported the limitation that their analysis was based on data from one published trial. They briefly mentioned the problems of generalising these results to the UK population.

Concluding remarks:
On the whole, the methods seem to have been reasonable and were adequately reported. The conclusions reached by
the authors appear to be appropriate.

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