The cost-effectiveness of bevacizumab in the first-line treatment of metastatic colorectal cancer in England and Wales

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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
The study determined the cost-effectiveness of adding bevacizumab to conventional chemotherapy strategies (irinotecan plus 5-fluorouracil/leucovorin or 5-FU/LV alone) for patients with untreated metastatic colorectal cancer in England and Wales. The study showed that bevacizumab was not likely to be cost-effective in the health care setting of England and Wales. The authors' conclusions, which were based on valid clinical and economic sources and appropriate methodology, are appropriate.

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

Study objective
The objective of the study was to determine the cost-effectiveness of adding bevacizumab to conventional chemotherapy strategies for patients with untreated metastatic colorectal cancer (CRC) in England and Wales. The current study represented an economic evaluation commissioned by the National Institute for Clinical Excellence (NICE).

Interventions
The interventions compared were bevacizumab added to irinotecan plus 5-fluorouracil (5-FU)/leucovorin (LV) (IFL) versus IFL alone, and bevacizumab plus 5-FU/LV versus 5-FU/LV alone. Bevacizumab was assumed to be given once per week at a dosage of 5 mg/kg for a duration of 6 or 8 weeks. All these options were used as first-line treatments.

Location/setting
England/Wales. Hospital.

Methods
Analytical approach:
The economic evaluation was based on a decision analytic model (probably a Markov chain) to determine the costs and benefits of the alternative strategies. The model was populated with published evidence. The perspective of the study was not explicitly stated but, given the study objective, was implicitly that of the National Health Service (NHS). The time horizon of the analysis was lifetime.

Effectiveness data:
Treatment effectiveness and other clinical data used in the model were derived from a systematic review of comparative randomised clinical trials (RCTs). The authors stated that details of the review and the studies were available in the full study report, which was published in a separate paper. However, key elements of each study (treatments compared and clinical results) were also reported in this article. The key clinical parameter was overall survival with each of the alternatives compared.

Monetary benefit and utility valuations:
The utility estimates used in the model were derived from systematic searches of the literature that identified evidence for specific health states considered in the model. No utility weights were available from the RCTs comparing the strategies under analysis, so only indirect evidence was found. No other details of the instruments and methods used to elicit preferences were provided.
Measure of benefit:
The summary benefit measures were the life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using the decision model. The use of discounting was not explicitly reported.

Cost data:
The analysis included the costs associated with drugs (acquisition and administration), diagnostic care, primary care visits, hospitalisation and best supportive care. The drug costs were derived from the British National Formulary, while the drug doses came from RCTs. Other resource use information was derived from the literature. The costs of health care services were based on typical UK published sources such as the Personal Social Services Research Unit. The price year was 2005. The use of discounting was not reported. The currency was UK pounds sterling (£).

Analysis of uncertainty:
Twelve alternative scenarios were considered in the deterministic sensitivity analysis. Model inputs such as utility scores, differential benefits of second-line therapy, lower and higher cost estimates, and different regimens were varied. A probabilistic sensitivity analysis was also undertaken by assigning probabilistic distributions to all uncertain model inputs through Monte Carlo simulation. This generated cost-effectiveness acceptability curves.

Results
The expected LYs and QALYs gained with bevacizumab plus IFL over IFL alone were 0.41 and 0.31, respectively. The incremental cost of adding bevacizumab was £19,361. Thus, the marginal cost per LY gained and per QALY gained was £46,853 and £62,857.

The expected LYs and QALYs gained with bevacizumab plus 5-FU/LV over 5-FU/LV alone were 0.19 and 0.18, respectively. The incremental cost of adding bevacizumab was £15,615. Thus, the marginal cost per LY gained and per QALY gained was £84,396 and £88,436.

The deterministic sensitivity analysis showed that the base-case results were quite robust to variations in clinical and economic inputs. The variables with the greatest impact were health utilities associated with pre- and post-progression health states, and the acquisition cost of bevacizumab. The probabilistic sensitivity analysis suggested that the probability that the cost-effectiveness of bevacizumab in either combination was better than £30,000 per QALY gained was close to zero.

Authors’ conclusions
The authors concluded that the addition of bevacizumab to conventional chemotherapy regimens for patients with CRC was not likely to be cost-effective in the health care setting of England and Wales.

CRD commentary
Interventions:
The rationale for the choice of the comparators was clear in that they represented widely used first-line treatments for CRC. The alternative chemotherapy regimens were explicitly described. They are also likely to be relevant comparators in other settings.

Effectiveness/benefits:
The clinical data were derived from a systematic review of the literature that identified head-to-head RCTs for the strategies compared. This represents a strength of the analysis and enhances the external validity of this study. The authors provided some details of these studies, although readers were often referred to the full Health Technology Assessment. Progression-free and overall survival were estimated using appropriate and standard statistical techniques (e.g. Kaplan-Meier curves). The authors noted that the clinical data were taken mainly from studies not conducted in the UK, thus the baseline risk could be different in England and Wales. However, hazard ratios were calculated and treatment effect is generally considered transferable among countries. Both LYs and QALYs were used as benefit measures, which represent adequate outcomes for the disease of interest. However, few details on utility weights were given in this article.

Costs:
Although the perspective of the study was not reported explicitly, the cost categories included and the institute that commissioned the analysis (NICE) suggest that the perspective of the UK NHS was used. The unit costs and dosages were reported for all of the drugs compared, while other costs were mainly reported as macro-categories. A clear list of the main categories of costs was provided. The authors did not state whether discounting was conducted, but it is likely that a 3.5% discount rate was used in accordance with NICE guidelines.

Analysis and results:
The authors provided a clear description of the model and its characteristics (i.e. health states, transition patterns, etc.). Base-case results and sensitivity analysis were reported extensively and clearly. Both deterministic and probabilistic sensitivity analyses were conducted, which appears appropriate given the study objective (to inform NICE). The authors acknowledged some limitation of the study which were mainly related to the lack of direct sources for utility weights and a lack of clinical data from England and Wales.

Concluding remarks:
The methodology of the study was very satisfactory and the reporting was clear and comprehensive. The authors’ conclusions are appropriate and were robust to the wide variations considered in the sensitivity analysis.

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Other publications of related interest


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