Cost-effectiveness of targeted therapy with cetuximab in patients with K-ras wild-type colorectal cancer presenting with initially unresectable metastases limited to the liver in a German setting

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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 objective was to assess the cost-effectiveness of cetuximab as first-line treatment for patients with the Kirsten rat sarcoma viral oncogene homologue (KRAS) wild type and metastatic colorectal cancer, with initially unresectable metastases, limited to the liver. The authors concluded that cetuximab plus fluorouracil, leucovorin, and irinotecan (FOLFIRI) was cost-effective, in Germany. The methods were good, and they and the results were adequately reported. Given the scope of the study, the authors' conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of cetuximab as first-line treatment for patients with the Kirsten rat sarcoma viral oncogene homologue (KRAS) wild type and metastatic colorectal cancer, in which the metastases were initially unresectable and limited to the liver.

Interventions
Fluorouracil, leucovorin, and irinotecan (FOLFIRI) with cetuximab was compared with fluorouracil, leucovorin, and oxaliplatin (FOLFOX) with bevacizumab.

Location/setting
Germany/out-patient secondary care.

Methods
Analytical approach:
A decision-analytic model was used to combine published data to predict the health outcomes and costs with each therapy. The time horizon was 10 years. The authors reported that the perspective was that of the German statutory health insurer.

Effectiveness data:
The effectiveness data were from published trials and cohort studies, and a Delphi panel. Due to the lack of head-to-head comparisons between cetuximab and bevacizumab, an indirect meta-analysis was undertaken, using the results of two separate clinical trials. These estimates were supplemented by expert opinion from the Delphi panel, which consisted of five German oncologists. The indirect comparison data were combined with survival models. The main effectiveness measures were overall survival and progression-free survival. These estimates were from trials identified by a literature review, conducted by the authors.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The measure of benefit was life-years gained and these were discounted at an annual rate of 5%.
Cost data:
The direct costs were those of the treatments (including medication and administration), out-patient care, ambulatory care provided by physicians, and in-patient care. The drug costs were based on treatment guidelines, product labels, and licenses. Out-patient costs were from German tariffs and in-patient costs were from diagnosis-related group data and expert opinion. The costs were discounted at an annual rate of 5% and reported in 2010 Euros (EUR).

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken by fitting normal distributions to each of the model parameters, except the costs, and varying them in 500 bootstrap simulations. One-way sensitivity analyses were conducted by varying all the model parameters, including the costs, over set ranges. The results were presented on a cost-effectiveness plane.

Results
The average cost per patient was EUR 99,134 with cetuximab and FOLFIRI compared with EUR 91,563 with bevacizumab and FOLFOX. The average life-years gained were 2.88 with cetuximab, compared with 2.38 with bevacizumab.

Compared with bevacizumab, cetuximab was associated with an incremental cost-effectiveness ratio of EUR 15,020 per life-year gained (95% CI 3,806 to 24,660).

The probabilistic analysis showed that at a willingness-to-pay of EUR 30,000 per life-year gained, cetuximab was cost-effective, compared with bevacizumab, in over 90% of simulations.

Authors' conclusions
The authors concluded that first-line treatment with cetuximab plus FOLFIRI was cost-effective in Germany for patients with the KRAS wild type.

CRD commentary
Interventions:
The interventions were reported clearly and appear to have been appropriate comparators.

Effectiveness/benefits:
The effectiveness data were from various sources and the methods of the indirect meta-analysis were described. A literature search was undertaken to identify the effectiveness sources, but the authors did not report if it was systematic, making it impossible to determine if all the relevant data were included. Due to a lack of identified data, the expert opinion of five German oncologists was sought and this should increase the validity of the results. The details of the methods used to derive the expert opinion were provided. The benefit measure appears to have been appropriate and was discounted.

Costs:
The perspective was explicitly reported and it appears that all the major costs relevant to the German statutory health insurer's perspective were analysed. The authors did not include the treatment costs that were paid either by the patient or by other insurance companies, as these were beyond the perspective adopted. The sources for the cost data were reported, as were the price year, time horizon, discount rate, and currency.

Analysis and results:
All the identified cost and outcome data were synthesised in a decision-analytic model. Details of the model were provided, including a diagram, but it was unclear if it was a tree or Markov model. The results were adequately presented. The uncertainty in the model was tested in one-way and probabilistic sensitivity analyses, but the costs were not varied in the probabilistic analysis. The reason provided was that the uncertainty in costs was only due to variations between German centres. It would have been useful to include these costs to assess the overall uncertainty in the model. The authors adequately reported the limitations of their study and the main one was that there was a lack of head-to-head evidence for the two interventions.
Concluding remarks:
The methods were good, and they and the results were adequately reported. Given the scope of the study, the authors' conclusions appear to be valid.

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