Cost-effectiveness of cetuximab in combination with irinotecan compared with current care in metastatic colorectal cancer after failure on irinotecan: a Belgian analysis

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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 investigated the cost-effectiveness of chemotherapy agents cetuximab plus irinotecan compared with current care for patients with epidermal growth factor receptor-expressing metastatic colorectal cancer. The authors concluded that cetuximab plus irinotecan was a cost-effective treatment and within acceptable thresholds in Belgium. Given the apparent quality and minimal reporting of the clinical evidence, it is not clear that the authors' conclusions were appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the medical costs and treatment effects of the chemotherapy regimen cetuximab plus irinotecan for patients with epidermal growth factor receptor-expressing metastatic colorectal cancer in Belgium.

Interventions
Cetuximab plus irinotecan was compared with current care for patients with epidermal growth factor receptor-expressing metastatic colorectal cancer, which had failed to respond to first-line irinotecan therapy. The chemotherapy regimens were administered for six or 12 weeks depending on tumour response; complete or partial response enabled further treatment beyond six or 12 weeks.

Location/setting
Belgium/out-patient care.

Methods
Analytical approach:
The analysis synthesised data from retrospective patient reviews and a key phase II randomised controlled trial; the BOND trial (Cunningham, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). The analysis covered the period from start of treatment until death, and the authors stated that the study perspective was that of the Belgium health care system.

Effectiveness data:
The clinical estimates included tumour response, time to progression, and survival. The evidence for clinical endpoints was abstracted from the BOND trial, which investigated the combination of cetuximab plus irinotecan compared with monotherapy cetuximab in metastatic colorectal cancer in Europe. For the cetuximab plus irinotecan combination, the clinical data came from one of the arms of the BOND trial. The clinical data for current care came from patients who met the inclusion criteria, but fell outside the recruitment period and were in the three largest BOND trial centres (Belgium, France and Italy).

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was life-years gained (LYG).
Cost data:
The direct medical costs were included and the cost categories were the cost of the drugs, laboratory tests, imaging, consultations, hospitalisations, subsequent treatments, and other medicines. The unit costs were presented and referenced. Data on resources used and their valuations were abstracted from patient records for a subset of Belgian patients from the BOND trial. Costs were presented in Euros (EUR) and the price year was not stated. Discounting was not applied due to the short time horizon.

Analysis of uncertainty:
Parameter uncertainty was addressed using one-way sensitivity analyses of the survival and cost parameters, for ranges ±1.96 times the standard error. These were reported separately by six-week or 12-week treatment assessments. Two-way analysis for survival and cost combinations was also performed and the results were presented in a table.

Results
For the Belgian health care system, costs for cetuximab plus irinotecan were EUR 18,340 for six-week or EUR 27,042 for 12-week treatment compared with EUR 13,450 for current care. The incremental costs were EUR 4,890 for six-week or EUR 13,592 for 12-week treatment, for cetuximab plus irinotecan. The incremental mean survival was 3.5 months for six-week and 4.05 months for 12-week treatment.

The incremental cost-effectiveness ratios were EUR 16,766 per LYG for six-week and EUR 40,273 per LYG for 12-week treatment compared with current care.

Sensitivity analyses showed that the base-case analysis results varied between EUR 28,924 for lower survival and higher cost (best scenario) and EUR 59,064 for higher survival and lower cost (worst scenario) for 12-week treatment before assessment.

Authors’ conclusions
The authors concluded that cetuximab plus irinotecan was a cost-effective approach compared with current care, in Belgium, for both the six- and 12-week treatment assessment scenarios.

CRD commentary
Interventions:
The dosage of the cetuximab plus irinotecan therapy was not stated. The current care was not described well and more detail of the specific treatments used and their frequency would have been useful.

Effectiveness/benefits:
The effectiveness data were derived from one key clinical trial, and the reasons for the selection of this trial were not clearly reported. Current care was not included in the trial; the clinical data for current care came from a group of patients, who met the inclusion criteria, but fell outside the recruitment period. Consequently, the benefits of randomisation were not possible. As details of this trial were minimally reported, an assessment on the validity of the clinical endpoints is not possible without recourse to the BOND trial report (Cunningham, et al. 2004).

Costs:
The direct medical costs were included and appear to have been appropriate to the perspective. It was unclear whether the costs for administering the chemotherapy drugs were included. Lower costs in the cetuximab plus irinotecan group were particularly driven by subsequent chemotherapy (post six- or 12-week assessment) in comparison with the current care. The sources of resource use, quantities of drug use, and unit costs were clearly presented. Although patient-level data on costs were used, statistical analyses do not appear to have been used to test for group differences, and nor were details of the cost distributions reported.

Analysis and results:
Incremental cost-effectiveness ratios were correctly calculated. The results and sensitivity analyses were not fully reported and only the two-way analysis results were presented. The authors noted that the efficacy for the treatment group in the trial was not dissimilar to that found in another study with a general clinical practice population, which suggested that the results may be applicable to such a setting. Limitations of the study were not discussed, but may have
included the small sample for the current care group, a lack of comprehensive statistical analysis on patient-level costs and outcomes, and a lack of multivariable sensitivity analysis.

Concluding remarks:
Given the apparent quality and minimal reporting of the clinical evidence, it is not clear that the authors' conclusions were appropriate.

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