Cost-effectiveness of second-line treatment with irinotecan or infusional 5-fluorouracil in metastatic colorectal cancer

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.

Health technology
Irinotecan was compared to infusional 5-fluorouracil (5-FU) as second-line treatment for patients with metastatic colorectal cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with metastatic colorectal cancer who had not responded to first-line treatment. No further details about the study population or the study sample were reported in this paper. The inclusion and exclusion criteria used in the clinical trial were not reported.

Setting
The study was based in tertiary care in France.

Dates to which data relate
The dates relating to the collection of effectiveness evidence and resources used were not reported. The price year was 1999.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Retrospective costing was carried out on the same sample of patients as that used for the effectiveness data.

Study sample
No power calculations or details about the method of sample selection were reported in this study. The study sample comprised 127 patients in the irinotecan arm and 129 in the 5-FU arm (39 in the Lokich regimen; 55 in the AIO regimen and 35 in the LV5-FU2 regimen).

Study design
This study was a multi-centre, randomised, controlled trial. The number of centres used for the study was not reported. No details about the method of randomisation were reported. The duration of follow-up was the total duration of patient survival or three-years, whichever was the shorter. The number of patients lost to follow-up was not reported. The blinding method for the assessment of outcomes was not reported.

Analysis of effectiveness
The basis for the analysis of effectiveness in clinical study (intention to treat or treatment completers only) was not stated. The study reported median rather than mean values. The primary health outcome used in the analysis was survival, which was measured from date of randomisation to death, whatever its cause, or last visit. No details about the comparability of groups or any adjustments for confounding factors were reported.

Effectiveness results
The median survival after treatment with irinotecan was 10.8 months compared to 8.5 months for patients treated with one of the three 5-FU regimens. This difference was reported to be statistically significant (p<0.035).

Clinical conclusions
The authors concluded that, in terms of improving survival, irinotecan is superior to 5-FU as a second-line treatment for patients with advanced colorectal cancer.

Modelling
Survival was estimated by a Kaplan-Meier method.

Measure of benefits used in the economic analysis
Survival was the measure of benefit used in the economic analysis.

Direct costs
Quantities and costs were measured but not reported separately for all of the resources included in the analysis. Direct costs were calculated only from the perspective of the hospital, which, in France, delivers the majority of healthcare for oncology patients. The costs included: chemotherapy, hospital admissions for administration of chemotherapy and for subsequent complications, and hospital outpatient clinic visits. The cost of symptom palliation was excluded because it was assumed that this would be equivalent in each treatment arm. The estimation of the quantities and costs was based on actual data recorded during the RCT. A time-and-motion study was used to estimate the time hospital staff spent in each management strategy (irinotecan or 5-FU). The unit cost for hospital admissions and tests were taken from the Henri Mondor and Pitie Salpetriere cost accounting system from Paris, France. Drugs and supplies were valued at the hospital purchase price. Costs were measured from the time of randomisation to the death of the patient or a three-year follow-up. Discounting was not carried out. The authors reported that this was because median survival was less than one-year and the largest part of the costs was incurred during the initial chemotherapy cycles. The dates relating to the measurement of the quantity of resources were not reported. The price year used to estimate the costs of hospital admissions and tests was 1998. The price year used to estimate the costs of other resources was not reported. The price year used to report the cost results was 1999. The authors did not report the methods used to adjust the unit costs to a common price year.

Statistical analysis of costs
There was no statistical analysis of costs.

Indirect Costs
Indirect costs were not reported because they were not consistent with the study perspective.
Currency
US dollars ($). The costs were calculated in French francs and converted to US dollars using the OECD purchasing power parity index.

Sensitivity analysis
Two one-way sensitivity analyses were carried out as follows: on the range for the gain in survival (range: 0.5 to 3.5 months), and on the cost of suppressing severe diarrhoea from the complications of irinotecan by using irinotecan plus LV5-FU2 chemotherapy. The cost of suppressing severe diarrhoea was estimated by adding the cost of LV5-FU2 chemotherapy and subtracting the cost of diarrhoea from the irinotecan arm.

Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
The total direct hospital costs per patient for irinotecan were $14,135. The total direct hospital costs per patient for 5-FU were: $12,192 for the Lokich regimen; $12,344 for the AIO regimen and $12,225 for the LV5-FU2 regimen. These costs included the costs of complications and adverse events of therapy, from initiation of therapy to death or end of follow up.

Synthesis of costs and benefits
The authors reported that, when the additional 2.3 months of improved survival were taken into account, the incremental cost-effectiveness ratios (ICERs) ranged from $9,344 to $10,137 per year of added survival. The study reported the incremental cost per year of added survival comparing irinotecan to each of the three 5-FU regimens.

The sensitivity analysis found that, when the benefit in survival ranged between 0.5 and 3.5 months, the ICERs ranged from $3,000 to $45,000 per year of added survival. When the cost of the combination regimen of irinotecan and LV5-FU2, proposed to suppress the cost of admissions for diarrhoea, was estimated, the ICER of irinotecan compared to the Lokich regimen became $29,373 per year of added survival.

Authors’ conclusions
The authors concluded that 5-FU regimens were the least expensive strategy for the management of metastatic colorectal cancer. However, the additional cost of using irinotecan was balanced by the added months of survival. The authors stated that the ICER of irinotecan was close to that of other cancer treatments.

CRD COMMENTARY - Selection of comparators
The selection of the three 5-FU regimens as comparators was reported to reflect current practice in Europe, which was based on published data from studies. However, before extrapolating the results to their local practice, decision-makers based in the UK should consider carefully whether the doses of chemotherapeutic agents, and use of folinic acid rescue therapy, reflect current practice in the NHS.

Validity of estimate of measure of effectiveness
The study did not report in detail the study design and methods used in the clinical trial of effectiveness. Therefore, it is not possible to assess the internal validity of the study and measures of effectiveness.

Validity of estimate of measure of benefit
The selection of survival as a measure of health benefit was appropriate to determine the number of months gained
from using irinotecan rather than 5-FU. The actual gain in survival was only 2.3 months but the authors pointed out that this equates to a 25% improvement for patients with advanced colorectal cancer who have 8.5 months life expectancy. The authors referred to 'patient refusal to continue chemotherapy' as a reason for stopping treatment. However, this study did not make any attempt to quantify the impact of patient preferences for the chemotherapeutic regimens used in this study or the no-treatment option. If more patients chose to discontinue therapy in one arm of the study, this may reflect differences in the value patients' place on the therapy received, and the effects of that therapy on their health and quality of life.

Validity of estimate of costs
The types of cost included in this study were appropriate to the chosen study perspective and setting. The authors excluded non-hospital health care costs and non-healthcare costs and indicated that the majority of oncology care was provided by the hospital sector in France. However, the authors did suggest that further studies are required to evaluate the costs of ambulatory care and non-healthcare costs. The study reported median rather than mean direct costs. Mean costs are the appropriate summary statistical measure to inform healthcare decision-making. The authors did not report all quantities and costs separately. The sources used for the resource use data were not clearly specified. The unit costs were estimated from cost accounting data for a tertiary care university hospital. The authors reported that these represented actual unit costs rather than charges. Sensitivity analyses of resource use and unit costs were not conducted.

Other issues
The authors did not compare the results of the evaluation with other published literature. The authors noted a number of factors that would affect the generalisability of the results of the study to other settings. These included the organisation and setting for the provision of supportive care after the failure of chemotherapy, the source of price data, the use of non-hospital health care services and non-health care services as part of the management of oncology patients.

The authors reported that the type of first-line treatment affected the selection of 5-FU regimen that was used in this study. However, no details were given regarding the types of first-line treatment patients received prior to this study.

Implications of the study
The authors suggested that irinotecan was the preferred strategy, based on cost-effectiveness, for the management of metastatic colorectal cancer when compared to 5-FU regimens. The authors cautioned that this study did not include ambulatory (such as patient transportation or nurse visits) or non-healthcare costs and further studies are required to estimate the impact of these costs.

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None stated.

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MeSH
Adenocarcinoma /diagnosis /drug therapy /economics /mortality /secondary; Adult; Aged; Antineoplastic Combined Chemotherapy Protocols /economics; Camptothecin /administration & dosage /analogs & derivatives /economics;