Costs of neoadjuvant chemotherapy and surgery in patients with liver metastases from advanced 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
The use of oxaliplatin combined with 5-fluorouracil and folinic acid (5-FU/FA), administered using the de Gramont regimen, for the treatment of patients with advanced colorectal cancer and metastasis confined to the liver.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced colorectal cancer and metastasis confined to the liver.

Setting
The setting was a hospital. The authors' economic study was carried out in the UK.

Dates to which data relate
The dates to which the effectiveness and resource data related were not reported. The price year was not given.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies.

Modelling
A decision analysis was carried out to estimate the average life-years gained, and the chemotherapy and surgical costs, of treating advanced colorectal cancer patients with liver metastases with either oxaliplatin combined with 5-FU/FA, or 5-FU/FA alone. One thousand patients with metastases confined to the liver were assumed to be treated with either oxaliplatin plus 5-FU/FA, or with 5-FU/FA alone, for 6 months. After that, it was assumed that the patients were assessed for suitability for resection, and those who had resectable metastases were operated on.

Outcomes assessed in the review
The outcomes assessed in the review were the resection rates, and the mean length of survival for resected and unresected patients with liver metastases initially considered unresectable.

Study designs and other criteria for inclusion in the review
No inclusion or exclusion criteria were reported. One of the studies was a randomised controlled trial, while the other was a retrospective, 9-year follow-up study.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Two primary studies were included in the review.

Methods of combining primary studies
The results of the individual primary studies were not combined. The authors obtained the resection rates from one of the studies, and the life-years gained per patient from the other.

Investigation of differences between primary studies
Not stated.

Results of the review
The resection rate for was 11.4% for oxaliplatin plus 5-FU/FA, and 4.1% for 5-FU/FA alone.

The number of life-years gained was 9 for a patient with resectable liver metastases after surgery, and 1.7 for a patient with unresectable liver metastases.

These results were included as input parameters in the decision model, in order to estimate the average and incremental life-years gained and the costs of chemotherapy and surgical resection.

Methods used to derive estimates of effectiveness
The authors made assumptions about the effectiveness.

Estimates of effectiveness and key assumptions
Data on the mean length of survival after surgery of those patients who survived the 9-year follow-up study (included in the review) were unavailable. The authors therefore assumed that the mean length of survival after surgery for these patients was equal to that of an age-matched normal population (21.6 years).

Measure of benefits used in the economic analysis
The summary measure of benefit was the number of life-years gained. The mean length of survival after surgery was assessed using the trapezoid method to calculate the area under the curve of a published survival curve with 9 years of follow-up (Giacchetti et al; see Other Publications of Related Interest).
Direct costs
Some of the resource quantities were reported separately from the costs. The direct costs included in the analysis were those of the health service. These included the drug acquisition costs ($9,216 for oxaliplatin and $3,276 for 5-FU/FA), the liver surgery costs for those who underwent surgery ($6,438), and the costs of the preoperative evaluation for those patients who did not undergo surgery ($314). The liver surgery costs included the preoperative evaluation, surgery, possible need for postoperative intensive/high-dependency care, a median postoperative in-hospital stay of 6 days (range: 3 - 15), and one postoperative outpatient attendance. The direct cost data were obtained from an unpublished study. The average and incremental costs were estimated using the decision model. Discounting was not carried out because it was irrelevant (the study period was less than 2 years). The price year was not reported.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
No indirect costs were reported.

Currency
UK pounds sterling (£).

Sensitivity analysis
A one-way sensitivity analysis was performed to analyse the robustness of the results when the resection rates were varied. The resection rates used in the sensitivity analyses were 27.3% for patients treated with oxaliplatin plus 5-FU/FA, and 9.8% for patients treated with 5-FU/FA alone. The first of these resection rates was obtained from a current published study, while the second was estimated using data from another published study. The authors also considered varying survival for those patients for whom data were unavailable, reducing it by 25% (to 16.2 years). The impact of discounting the survival gain by 1.5% was also considered. The area of uncertainty investigated was variability in the data.

Estimated benefits used in the economic analysis
The total life-years gained for a cohort of 1,000 patients was 2,532 for treatment with oxaliplatin plus 5-FU/FA, and 1,999 for treatment with 5-FU/FA alone.

Cost results
The average cost per patient was £10,228 for treatment with oxaliplatin plus 5-FU/FA, and £3,841 for treatment with 5-FU/FA alone.

For the sensitivity analysis in which the resection rates were varied, the average cost per patient was £11,202 for treatment with oxaliplatin plus 5-FU/FA, and £4,190 for treatment with 5-FU/FA alone.

Synthesis of costs and benefits
The incremental cost per life-year gained was calculated as the extra cost of treatment with oxaliplatin plus 5-FU/FA, compared with that of 5-FU/FA.

In the baseline case, the incremental cost per life-year gained with oxaliplatin plus 5-FU/FA, compared with 5-FU/FA alone, was £11,985.

When the more optimistic resection rates were varied in the sensitivity analysis, the cost per life-year gained when using oxaliplatin plus 5-FU/FA, compared with 5-FU/FA alone, was £5,489.
When the survival rate for those patients for whom data were unavailable was reduced by 25% (to 16.2 years), the cost per life-year gained with oxaliplatin plus 5-FU/FA, compared with 5-FU/FA alone, was 15,624.

When the benefits were discounted by 1.5%, the cost per life-year gained with oxaliplatin plus 5-FU/FA, compared with 5-FU/FA alone, was 12,867.

**Authors' conclusions**

Oxaliplatin plus 5-fluorouracil and folinic acid (5-FU/FA) is the only first-line treatment that has the possibility of increasing resection over 5-FU/FA alone, allowing a higher long-term survival for those patients with unresectable colorectal cancer metastases confined to the liver, at an acceptable cost.

**CRD COMMENTARY - Selection of comparators**

A justification was given for the comparator, 5-FU/FA. 5-FU/FA is a widely used treatment for advanced colorectal cancer in the UK. You should decide if this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The authors did not carry out a systematic review of the literature. They used data from the two studies selectively. Therefore, the conclusions of the study depend heavily on the accuracy of the data derived from the primary studies. The authors also made an assumption about the survival for some patients for whom the data were unavailable data, but they did not provide any evidence for the choice of the value adopted. However, the estimates were investigated by sensitivity analyses, which seem to have been appropriate.

**Validity of estimate of measure of benefit**

The estimation of the benefits was reported as the patient-years gained with the therapies under study. The life-years gained were modelled using a decision model, which seems to have been appropriate for the study question. After comparing the results obtained with those from other studies, the authors reported that the data used for modelling the costs and benefits of the interventions were conservative. Moreover, they argued that the study was likely to have overestimated the benefits derived from treatment with 5-FU/FA alone. People receiving this therapy have shorter survival, and this may lead them to perceive a lower quality of life.

**Validity of estimate of costs**

All the categories of costs relevant to the perspective adopted appear to have been included in the analysis. The costs relating to the administration of 5-FU/FA were excluded. This does not seem to have affected the results since these costs were common to both therapies. The authors reported that the timeframe of the analysis was short, and the long-term costs of treatment following the point at which a patient was considered for resection were excluded. This may have biased the results of the study. In addition, the authors stated that this approach underestimated the costs of those non-resected patients who would need palliative care for approximately 1.7 years, and also the costs of those patients who received curative resections. They argued that these latter costs were likely to have less impact on the total costs than the costs related with palliative care. Therefore, the study is likely to have favoured treatment with 5-FU/FA alone.

Some of the quantities were reported separately from the costs, but a full report would have improved transparency. A sensitivity analysis of the quantities was not reported, which may limit the interpretation of the study findings. Also, no sensitivity analysis of the prices was reported. The lack of a price year hinders reflation exercises to other settings. The incremental analysis was carried out correctly.

**Other issues**

The authors made appropriate comparisons of their findings, in terms of resection rates and survival, with those from other studies. The issue of generalisability to other settings was not addressed. The authors do not seem to have presented their results selectively, except with some lack of costing.
Implications of the study
The authors reported that the use of oxaliplatin plus 5-FU/FA can help to achieve one of the Governments’ commitments. Cancer deaths could be reduced by 10% by the year 2010, by increasing the survival and the resectability of those patients with advanced colorectal cancer with unresectable metastases confined to the liver. Whether this is at an acceptable cost, as they claim, depends also on whether there is any loss of benefit on account of diverting resources to fund this treatment, that is, the opportunity costs.

Source of funding
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Bibliographic details

Other publications of related interest
Alberts SR, Horvath WL, Donohue JH, et al. Oxaliplatin (OXAL), 5-fluorouracil (5FU), and leucovorin (CF) for patients (pts) with liver only metastases (mets) from colorectal cancer (CRC): a North Central Cancer Treatment Group (NCCTG) phase II study. American Society of Clinical Oncology; 2001.


Indexing Status
Subject indexing assigned by CRD

MeSH
Adenocarcinoma /drug therapy; Antineoplastic Combined Chemotherapy Protocols /therapeutic use /economics; Colorectal Neoplasms /drug therapy; Cost-Benefit Analysis; Drug Administration Schedule; Fluorouracil /administration & dosage /economics; Liver Neoplasms /drug therapy /secondary /surgery; Organoplatinum Compounds /administration & dosage /economics; Treatment Outcome

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