Effectiveness and cost-effectiveness of peri-operative versus post-operative chemotherapy for resectable colorectal liver metastases

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 chemotherapy before and after hepatectomy (perioperative) versus chemotherapy only after hepatectomy (postoperative), for patients with resectable colorectal liver metastases. The authors concluded that perioperative chemotherapy could be cost-effective as it avoided hepatic resection for patients who did not respond to chemotherapy; the expected survival with perioperative or postoperative chemotherapy was similar. The cost-effectiveness methods were conventional and the authors’ conclusions appear to be robust.

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

Study objective
The objective was to assess the cost-effectiveness of chemotherapy before and after hepatectomy (perioperative) versus chemotherapy only after hepatectomy (postoperative), for patients with resectable colorectal liver metastases.

Interventions
Perioperative chemotherapy was administered before and after hepatectomy, while postoperative chemotherapy was only administered after hepatectomy. Chemotherapy consisted of leucovorin (folinic acid), fluorouracil, and oxaliplatin in the FOLFOX4 regimen.

Location/setting
Italy/hospital.

Methods
Analytical approach:
The analysis was based on a Markov model with a 10-year time horizon. The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data were identified by a review of the literature in MEDLINE and EMBASE, by two investigators. Studies of perioperative or postoperative chemotherapy, or both, for patients receiving hepatectomy, were selected. The sample size and results for each study were reported, and pooled estimates were calculated where there were multiple sources. The key clinical input was the three-year recurrence-free survival (RFS).

Monetary benefit and utility valuations:
The utility values for chemotherapy and its side effects were from published literature.

Measure of benefit:
Life-months and quality-adjusted life-months (QALMs) were the summary benefit measures. They were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of in-patient and out-patient visits, diagnostic and laboratory tests, medications, procedures, such as hepatic resection and hepatectomy, and the treatment of adverse events, such as
diarrhoea and neutropenia. The unit costs were based on payments made by the Italian public health care system. The
drug costs were their average wholesale prices. All costs were in Euros (EUR) and the price year was 2010. A 3%
annual discount rate was applied.

Analysis of uncertainty:
One- and two-way sensitivity analyses were carried out on the model inputs. The ranges of values for the clinical inputs
and utilities were from published sources. The costs were varied by ±20% of their base-case values.

Results
Over 10 years, the expected life-months were 54.56 with perioperative and 52.62 with postoperative chemotherapy.
The QALMs were 39.33 with perioperative and 37.84 with postoperative chemotherapy. The costs per patient were
EUR 27,054 with perioperative and EUR 25,874 with postoperative chemotherapy.

The average cost per life-month gained was EUR 495.9 with perioperative chemotherapy and EUR 491.7 with
postoperative chemotherapy. The average cost per QALM gained was EUR 687.9 with perioperative and EUR 683.8
with postoperative chemotherapy.

The incremental cost per QALM gained with perioperative chemotherapy, over postoperative chemotherapy, was EUR
791.9. This was lower than the cost-effectiveness threshold of EUR 3,000 per QALM, equivalent to EUR 50,000 per
quality-adjusted life-year.

The three-year RFS with perioperative chemotherapy was the main driver of model. The incremental cost per QALM
gained with perioperative chemotherapy ranged from EUR 448.1 when the RFS was 36.8% to EUR 8,075 when the
RFS was 31.5%. The three-year RFS with postoperative chemotherapy had an impact on the cost-effectiveness results,
as did the cost of hepatic resection.

Authors' conclusions
The authors concluded that perioperative chemotherapy could be cost-effective as it avoided hepatic resection for
patients who did not respond to chemotherapy; the expected survival with perioperative or postoperative chemotherapy
was similar.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the best chemotherapy strategy for these patients was unclear.

Effectiveness/benefits:
A valid approach was used to identify the relevant sources of evidence. The methods of the literature review were
given, as were the sample size and results of each study, but the design of each study was not. This makes it impossible
to judge the validity of the clinical inputs. The authors stated that studies were selected on the basis of their level of
evidence, as defined by the US Preventive Services Task Force. Plausible ranges of values were tested in the sensitivity
analyses. The derivation of utility values was not reported. Months of life were an appropriate benefit measure given
the poor survival of patients with this type of cancer. Quality adjustments were relevant because of the side-effects of
chemotherapy.

Costs:
The authors stated that the analysis was conducted from a societal perspective, but they focused on the direct medical
costs relevant to the public health payer. These costs were from official reimbursement data. Most of them were
presented as category totals and were not broken down into individual items. Limited information on the resource
quantities was provided. The price year was reported, allowing reflation exercises for other time periods. The impact of
variations in the cost estimates was tested in the sensitivity analyses.

Analysis and results:
The results were clearly presented and the projected costs and benefits were synthesised using an incremental approach.
A conventional cost-effectiveness threshold was used to identify the best strategy. The uncertainty was investigated,
using a deterministic approach, and the methods and results were clearly reported and discussed. The authors
acknowledged that the costs might have varied by geographical area and clinical management, and they might not be transferable to other settings. They pointed out that the costs for perioperative chemotherapy depended on the additional costs of chemotherapy and of higher morbidity and prolonged in-patient stay for these patients, but costs were saved by patients becoming unresectable during chemotherapy before surgery.

Concluding remarks:
The cost-effectiveness methods were conventional and the authors’ conclusions appear to be robust.

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