Randomised trial comparing epirubicin, cisplatin, and fluorouracil versus fluorouracil, doxorubicin, and methotrexate in advanced esophagogastric 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
Using either ECF regimen (the combination of epirubicin, cisplatin and protracted venous infusion fluorouracil (5-FU)) or FAMTX (the standard combination of 5-FU, doxorubicin and methotrexate) in patients with advanced esophagogastric cancer.

Type of intervention
Treatment and palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with advanced esophagogastric cancer, whose bone marrow functioned adequately, who had creatinine clearance >40 mln., whose life expectancy was at least 3 months, and who experienced no concurrent uncontrolled illness.

Setting
Hospital. The economic study was carried out in the United Kingdom.

Dates to which data relate
The effectiveness data were collected during the period from July 1992 to June 1995. The resource data were gathered for the period of chemotherapy treatment plus 2 months posttreatment. The years during which the price data were collected were not specified.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on a subgroup (120 patients) of the patient sample used in the effectiveness analysis from one institution.

Study sample
Power calculations were used to determine the sample size. A total of 274 patients were randomly assigned to either the ECF group or the FAMTX group (137 in each group). 18 patients (6.57%) were excluded following which the ECF group numbered 126 patients versus 130 in the FAMTX group.
Study design
The study was a multicentre randomised controlled trial that was carried out in eight centres. A non-stratified randomisation method was used. The median follow-up duration of the study sample was 6.1 months. In the calculation of response rate the overall loss to follow up was 14.45% (11.9% in the ECF group versus 16.9% in the FAMTX group).

Analysis of effectiveness
The analysis of the clinical study was based on intention to treat (except in the calculation of response rate). The primary health outcomes used in the analysis were survival time and rate, response rate, toxicity and quality of life. A questionnaire from the European Organisation for Research and Treatment of Cancer [EORTC] QLQ-C30 was used to assess the quality of life. The patient characteristics in the two study groups were shown to be comparable. A multivariate analysis was conducted to identify the factors correlated with poor survival.

Effectiveness results
The ECF group had a median survival time of 8.9 months versus 5.7 months for the FAMTX group (p=0.0009). The ECF group had a one-year survival rate of 36% (95% CI: 27% - 45%) versus 21% (14% - 29%). The corresponding figures for two-year survival rate were 11% (6% - 19%) and 6%, respectively. The ECF group had a response rate of 45% (95% CI: 36% to 54%) versus 21% (95% CI: 13% to 29%) for the FAMTX group (p=0.0002). With regard to toxicity, the percentage of patients experiencing treatment delays and dose reductions was 32% in the ECF and 41% in the FAMTX group. The patients in the FAMTX group experienced more overall mucositis and nephrotoxicity, as well as more overall and severe hematologic toxicity and infections. However, the ECF regimen group experienced more severe emesis and alopecia. With regard to the global quality of life scores, the study revealed no significant difference between the groups at 12 weeks (p=0.71) but at 24 weeks the ECF group had higher scores relative to the FAMTX group (p=0.04). The multivariate analysis revealed that poor survival was correlated with metastatic disease (hazards ratio (HR), 1.61; 95% CI: 1.17 to 2.20) and performance status greater than or equal to 2 (HR, 1.76; 95% CI: 1.26 to 2.45) as well as FAMTX chemotherapy.

Clinical conclusions
The authors concluded that "the ECF regimen results in a superior response rate and survival when compared with FAMTX with less myelo-suppression and better quality of life".

Measure of benefits used in the economic analysis
The survival time was the outcome measure used in the economic analysis.

Direct costs
Quantities and costs were not reported separately. The total cost per patient was calculated as the main measure of cost analysis. The cost components consisted of the costs of chemotherapy, nonchemotherapy drugs, central venous lines, delivery pumps, pathology and radiology tests, inpatient time, outpatient consultations, day ward and operating room time. The costs were calculated from a hospital's perspective. The source of the cost data on 120 patients was one of the study sites. The date to which price data referred was not specified. The costs of local palliative care after chemotherapy, other primary care, or nonprofessional care providers were omitted since they were common to both health technologies.

Indirect Costs
Not included.

Currency
Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
The ECF group had a median survival time of 8.9 months versus 5.7 months for the FAMTX group (p=0.0009).

Cost results
The ECF group had average total costs of $13,760 versus $13,500 in the FAMTX group. The costs of side effects were included in the cost analysis.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio. The ratio was the result of dividing the difference in the average total costs by the difference in survival time between the alternative health technologies. The incremental cost of ECF was $975 per year of life gained.

Authors' conclusions
This study demonstrates that the ECF regimen should be regarded as the standard treatment in advanced esophagogastric cancer. It can be offered to all patients with reasonable performance status based on the evidence of survival advantage, tolerable toxicity, maintenance of quality of life and cost-effectiveness when compared with the FAMTX regimen.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator. FAMTX was chosen as the comparator since clinical trials had established its superiority or equivalent effectiveness relative to its rivals. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of benefit
The estimate of the measure of benefit used in the economic analysis is likely to be internally valid.

Validity of estimate of costs
Resource quantities were not reported separately from the prices. Adequate details of the methods of quantity/cost estimation were not given.

Other issues
In view of the lack of sensitivity analysis and statistical analysis of costs, the results may not be generalisable to other settings.

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