Patterns, costs and cost-effectiveness of care in a trial of chemotherapy for advanced non-small cell lung 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 mitomycin, ifosfamide and cisplatin chemotherapy (MIC) combined with palliative care (PC) in non-small-cell lung cancer (NSCLC).

Type of intervention
Treatment and palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced NSCLC. The patients included in the trial were characterised as being ambulatory patients (WHO performance status 0, 1 or 2), aged 75 years or less, with inoperable extensive stage NSCLC.

Setting
The setting was a health authority area. The economic study was carried out in South Birmingham Health Authority area, UK.

Dates to which data relate
The effectiveness data and the resource quantities were collected between March 1988 and March 1996. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a single study. The results of the randomised trial performed in the single study had been published in another paper by the same authors (see Other Publications of Related Interest).

Link between effectiveness and cost data
The resource quantities were collected retrospectively for the same patient sample as that used in the single study.

Study sample
No power calculations to determine the sample size were reported. The authors presented baseline characteristics as evidence that the study sample was representative of the study population. In total, 351 eligible patients were recruited for the trial. A subset of 116 patients was used for this analysis (58 in each treatment arm). The authors noted that the details of the trial were reported in the other publication (see Other Publications of Related Interest).
Study design
The study was a randomised controlled trial. It may have been multi-centre because consultants from the South
Birmingham Health Authority area treated the patients included in the effectiveness analysis. The method of
randomisation used to allocate the patients was not reported. The duration of follow-up was from entry into the trial
until death or last follow-up for all the patients. Of the 116 patients included in the study, 82 (71%) had complete data,
11% of the patients had one set of unobtainable medical notes, 18% had two or more, and one patient had no
retrievable notes. The 82 patients with complete data comprised 39 in the MIC+PC group (representing 68% of the
individuals within this group), and 43 in the PC group (representing 74% of patients in this group). The authors stated
that the missing data were unrelated to the characteristics of the patients, although they did not provide any evidence to
support this.

Analysis of effectiveness
The authors did not report whether the analysis of effectiveness was conducted on an intention to treat basis or on
treatment completers only. However, given the incompleteness of the records, it appears to have been based on
intention to treat. The primary health outcomes used in the analysis were:

the hazard ratio of MIC+PC against PC;

the mean survival with MIC+PC and with PC; and

the place of death for the patients, in terms of the number (and percentage) of patients in each treatment arm who died
either at home, in the hospital, in the hospice, in another place, unknown or not applicable (being still alive at the end of
the study).

The groups were shown to be comparable at analysis in terms of their age, gender, histology and WHO performance
status at the beginning of the study.

Effectiveness results
The hazard ratio of MIC+PC against PC was 0.79 (95% confidence interval, CI: 0.63 - 0.97; P=0.03).

The mean survival time with MIC+PC was 9.6 months (95% CI: 7.8 - 11.4), compared with 7.2 months (95% CI: 6.1 -
8.2) with PC.

For the patients in the MIC+PC treatment group,

22 (38%) died at home,
22 (38%) died in the hospital,
7 (12%) died in the hospice,
4 (7%) died in other places,
for 2 (3%) the place of death was unknown, and
there was one patient (2%) still alive at the end of the study.

Among the patients under PC,

22 (38%) died at home,
15 (26%) died in the hospital,
16 (28%) died in the hospice,  
2 (3%) died in other places, and  
for 3 (5%), the place of death was unknown.

**Clinical conclusions**  
The hazard ratio was statistically significantly different from 1 in favour of the intervention. The intervention produced a longer survival, although not statistically significant at the 5% level. Regarding the place of death, a greater proportion of patients in the MIC+PC group died in the hospital, compared with PC patients. The proportion of PC patients who died in a hospice was higher in comparison with the MIC+PC patients.

**Measure of benefits used in the economic analysis**  
The measure of benefits used was the life-months (years) gained. The mean survival was determined by calculating the area under the Kaplan-Meier curve using the trial data.

**Direct costs**  
The resource quantities and the unit costs were reported separately. The direct costs included in the analysis were those related to the hospital, the community and hospice resources. Associated with these, the resources per patient were hospital inpatient days related and unrelated to chemotherapy, outpatient visits, MIC chemotherapy courses, radiotherapy fractions, general practitioner (GP) surgery visits, GP or consultant home visits, district nurse or hospice care nurse or hospice care team visits, hospice inpatient days, and hospice outpatient visits. The costs were estimated using actual data derived from the National generic cost (1999), the Queen Elizabeth Hospital Pharmacy and Radiotherapy Departments (1999), and the St. Mary's Hospice (1999). The costs were calculated for those patients with complete data, and then regression imputation was performed to calculate the costs for the whole sample. The authors reported the average and incremental costs. Discounting was not carried out but was irrelevant because, as the authors stated, the survival for the majority of the patients was less than 12 months. Therefore, the costs were incurred over less than 2 years.

**Statistical analysis of costs**  
Non-parametric stratified bootstrapping was applied to calculate the CIs for the difference in means.

**Indirect Costs**  
No indirect costs were reported. If a societal perspective was to be adopted, the indirect costs (for example, those costs related with the care provided by relatives) should be included in the analysis.

**Currency**  
UK pounds sterling (£).

**Sensitivity analysis**  
No sensitivity analysis was reported.

**Estimated benefits used in the economic analysis**  
The number of months gained with MIC+PC in comparison with PC was 2.4.

**Cost results**
When patients with complete data were considered, the total cost ranged from 1,247 to 18,182 for the MIC+PC arm, compared with 324 to 12,498 for the PC arm.

The mean cost for the MIC+PC arm was 6,999 (standard deviation, SD=4,194) compared with 4,076 (SD=3,078) for the PC arm.

Applying bootstrapping for all the patients with complete data gave a mean cost difference of 2,924 (95% CI: 1,234 - 4,323).

When regression imputed values were included, the mean cost for the 58 patients included in the MIC+PC arm was 7,198 (SD=3,776), compared with 3,933 (SD=2,683) for the 58 patients included in the PC arm.

The difference in the mean cost between the treatment arms, obtained by applying bootstrapping of all 116 patients, was 3,264 (95% CI: 2,093 - 4,446).

In the MIC+PC group:

the total number of hospital inpatient days was 17.8 (SD=14.6), the number of hospital inpatient days related to chemotherapy was 6.2 (SD=7.2), and the number of hospital inpatient days unrelated to chemotherapy was 11.6 (SD=13.1);

the number of outpatient visits was 5.6 (SD=4.6);

the number of courses of MIC chemotherapy was 2.7 (SD=1.5);

the number of radiotherapy fractions was 5.6 (SD=6.5);

the number of GP surgery visits was 12.3 (SD=13.3);

the number of GP or consultant home visits was 1.6 (SD=3.1);

the number of district nurse or hospice care nurse or hospice care team visits was 2.2 (SD=4.9);

the number of hospice inpatient days was 2.5 (SD=7.5); and

the number of hospice outpatient visits was 0.8 (SD=2.2).

In the PC group:

the total number of hospital inpatient days coincided with the number of hospital inpatient days unrelated to chemotherapy, and was 6.9 (SD=10.7);

the number of outpatient visits was 5.5 (SD=4.1);

the number of radiotherapy fractions was 6.8 (SD=5.4);

the number of GP surgery visits was 11.9 (SD=11.2);

the number of GP or consultant home visits was 0.8 (SD=2.2);

the number of district nurse or hospice care nurse or hospice care team visits was 2.6 (SD=7.6);

the number of hospice inpatient days was 3.8 (SD=7.6); and

the number of hospice outpatient visits was 0.3 (SD=1.3).
Synthesis of costs and benefits
The 2.4 months' gain in mean survival with MIC+PC was at a cost of 2,924. Therefore, the incremental cost-effectiveness ratio was 1,218 per life-month gained (95% CI: 514 - 1,801) or 14,620 per life-year gained (95% CI: 6,168 - 21,612). The authors reported that similar results were obtained when imputed values were included.

Authors' conclusions
The survival benefits for mitomycin, ifosfamide and cisplatin chemotherapy (MIC) combined with palliative care (PC) were only achieved with additional costs, due mainly to the greater use of hospital resources by MIC+PC patients. The authors stated that a judgement has to be made to decide whether, on average, the investment of 2,924 is justified by the achievement, on average, of 2 months' life, for patients with non-small-cell lung cancer (NSCLC).

CRD COMMENTARY - Selection of comparators
The authors did not provide a justification for the choice of PC, as opposed to any other technologies, as the comparator. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis used a randomised controlled trial, which was appropriate for the study question. The baseline characteristics were presented to test whether the study sample was representative of the study population. The patient groups were shown to have been comparable at analysis. While the effectiveness information was reported elsewhere, the transparency would have been improved by reporting the loss to follow-up more clearly. It was clear, in terms of the resource use data, but not for the effectiveness (survival) data.

Validity of estimate of measure of benefit
The estimation of benefits (life-months gained) was derived from the area under the Kaplan-Meier curve using the trial data. This is a method commonly used in studies that estimate survival as the measure of benefit of the analysis. As the authors correctly pointed out, there was no problem with estimating mean survival due to right censoring if all the patients died during the study period.

Validity of estimate of costs
It appears that all the categories of cost relevant to the perspective adopted (health care system) were included in the analysis. Although there were missing data for some patients for the calculation of the costs, the authors stated that this was reasonably balanced across the two treatment arms. Therefore, bias in the study due to these missing data is unlikely. Moreover, the regression imputation showed that the results were very similar to those obtained only for patients with complete data. The unit costs and the quantities were reported separately, which enhances the reliability of the conclusions and the generalisability. The mean and standard deviation were given for the resource quantities used in the analysis. The unit costs were obtained from published sources. No sensitivity analyses of the prices were performed but the price year was given, which facilitates reflation exercises to other settings.

Other issues
The authors made appropriate comparisons of their findings with those from a similar study carried out in Canada (see Other Publications of Related Interest). In the Canadian study the average number of hospital inpatient days for PC patients was much higher than for this study and, therefore, PC was more expensive than cyclophosphamide, adriamycin and cisplatin chemotherapy. The authors stated that this might have been due to the fact that the Canadian health care system is more hospital orientated than the UK NHS. The issue of generalisability of the results to other settings was not addressed. The results were generally reported in full, although some details were probably available in the other publication. The issue of generalisability was not addressed, although the authors' conclusions were in keeping with the scope of the study.
Implications of the study
The results of this study show that the consideration of MIC+PC as a cost-effective treatment, compared with PC alone, depends partly on the judgement made by the policy maker about how valuable it is to spend 2,924 to provide two extra months of life for patients with NSCLC. Moreover, the cost-effectiveness of MIC+PC in comparison with PC alone is highly dependent on how hospital orientated the national health service under study is. The higher the hospital orientation of PC in a health system, the more likely it is that the MIC+PC treatment will be cost-effective.

Source of funding
Funded by the National Health Service Research and Development Programme.

Bibliographic details

PubMedID
12140146

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy /economics /pathology; Cisplatin /economics /therapeutic use; Costs and Cost Analysis; Female; Home Care Services, Hospital-Based /economics; Hospital Costs; Hospitalization /economics; Humans; Ifosfamide /economics /therapeutic use; Length of Stay; Lung Neoplasms /drug therapy /economics /pathology; Male; Middle Aged; Mitomycin /economics /therapeutic use; Palliative Care /economics; Prospective Studies; Retrospective Studies; Sensitivity and Specificity; Treatment Outcome

AccessionNumber
22002001537

Date bibliographic record published
28/02/2003

Date abstract record published