Paclitaxel plus carboplatin, compared with paclitaxel plus gemcitabine, shows similar efficacy while more cost-effective: a randomized phase II study of combination chemotherapy against inoperable non-small-cell lung cancer previously untreated


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 two combination treatments for patients with inoperable non-small-cell lung cancer (NSCLC). The treatments were paclitaxel plus carboplatin (PC) and paclitaxel plus gemcitabine (PG). In the PC group, paclitaxel (175 mg/m2) was given as a 3-hour intravenous infusion, followed by carboplatin intravenously (AUC = 7) for 1 hour on day 1 every 3 weeks. In the PG group, paclitaxel (175 mg/m2) was given intravenously on day 1, while gemcitabine (1,000 mg/m2) was administered intravenously for 30 minutes on days 1 and 8 every 3 weeks. The treatment regimens were modified when required.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with the following characteristics:

- a cytological or histological diagnosis of locally advanced (stage IIIb, including those with malignant pleural effusions) or metastatic (stage IV) NSCLC;
- age between 18 to 80 years;
- no prior chemotherapy, radiotherapy or immunotherapy;
- a performance status of 0 to 2 on the World Health Organization (WHO) scale;
- bidimensionally measurable disease;
- adequate bone marrow reserve with a blood cell count of at least 4,000/mm3, a platelet count of at least 100,000/mm3, and a haemoglobin level of at least 10 g/dL; and
- female patients with appropriate contraception.

Patients were excluded if they presented signs or symptoms of brain metastases, a recent myocardial infarction more than 3 months before the date of diagnosis, unstable angina, inadequate liver function (bilirubin greater than 1.5 times and ALT/AST greater than 3 times the upper normal limit), or inadequate renal function with creatinine greater than 2.0 mg/dL. Patients with a second primary malignancy, except in situ carcinoma of the cervix or adequately treated basal cell carcinoma of the skin, were also excluded.
Setting
The setting was a hospital. The economic study was carried out at the Taipei Veterans General Hospital, National Yang-Ming University in Taiwan.

Dates to which data relate
The effectiveness evidence and resource use data were gathered from August 1999 to August 2000. No price year was reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
The study was designed to enrol 90 qualified patients (45 in each arm), to determine whether there was a statistically significant difference in the time required for treatments in the two regimens, such that the lower limit of the 95\% confidence interval (CI) was higher than 20\% for the response rates of the treatments. During the study period, 90 patients were selected. There were 45 patients in the PC group and 45 in the PG group. The mean age in the PC group was 64 years (range: 37 - 77) and 35 patients were men. The mean age in the PG group was 67 years (range: 35 - 80) and 33 patients were men. No patient was excluded from the initial sample.

Study design
This was a phase II randomised controlled trial, which was carried out in a single centre (Taipei Veterans General Hospital in Taiwan). The randomisation process used a computer-generated list of random numbers and was carried out by a statistical office not involved in the trial. The median follow-up was 15 months and the loss to follow-up was not reported. Blinding was not assessed.

Analysis of effectiveness
All patients included in the study were accounted for in the analysis. Thus, the basis of the clinical analysis was intention to treat. The primary health outcomes were:

- complete response, in other words disappearance of all known disease (determined by two observations no less than 4 weeks apart;
- partial response, that is, a decrease of greater than 50\% in the total tumour size of the measurable lesions (determined by two observations no less than 4 weeks apart), with no appearance of new lesions or progression of any lesion;
- the progression or stability of the disease, time to disease progression and survival (calculated using Kaplan-Meier survival estimates during the follow-up period);
- management of pain, dyspnoea, cough, and haemoptysis; and
- haematological and non-haematological toxicities.

The study groups were comparable at baseline in terms of the demographics and clinical conditions.

Effectiveness results
Complete response was obtained in 3 patients (6.7%) in the PC group and in no patients in the PG group.

Partial response was obtained in 15 patients (40%) in the PC group and in 18 patients (40%) in the PG group.

Overall response (complete response plus partial response) was thus similar in both study groups and applied to 18 patients (40%).

The response rate was not correlated with the patient's performance status and staging.

The disease was stable in 22 patients (48.9%) in the PC group and in 20 patients (44.4%) in the PG group.

The disease progressed in 5 patients (11.1%) in the PC group and in 7 patients (15.6%) in the PG group.

The median time to disease progression was 5.7 months in the PC group and 6.2 months in the PG group.

The median survival time was 14.1 months (95% CI: 6.3 - 21.8) in the PC group and 12.6 months (95% CI: 7.6 - 17.5) in the PG group.

One-year survival was 50.7% in the PC group and 53.5% in the PG group.

Pain control was improved in 7 out of 22 patients in the PC group, and in 13 out of 29 in the PG group. Dyspnoea abated in 14 out of 21 patients in the PC group and in 15 out of 31 in the PG group. Coughs were reduced in 15 out of 24 patients in the PC group, and in 12 out of 20 in the PG group. Haemoptysis was resolved in 4 out of 5 patients in the PC group and in 2 out of 3 in the PG group.

In terms of the WHO grade 3 or 4 haematological toxicities, leucopenia occurred in 6 patients (13.3%) in the PC group and in 4 (8.9%) in the PG group, anaemia occurred in 6 patients in each group (15.5% PC and 13.3% PG), and thrombocytopenia occurred in 5 patients (11.1%) in the PC group and in none in the PG group. Finally, non-haematological toxicities were mild and were tolerated in both groups.

Clinical conclusions
The authors concluded that the toxicity profile, response rate and survival were similar, but not equal, in the two study groups.

Measure of benefits used in the economic analysis
Since no summary benefit measure was used, and the authors considered the health outcomes to be similar, a cost-minimisation analysis was therefore carried out.

Direct costs
Discounting was not carried out since the costs were incurred over one year. The quantities of resources were reported, but the unit costs were not. The cost items included in the analysis referred to hospitalisation, drugs, chemotherapy, outpatient visits, and emergency room visits. The cost/resource boundary adopted appears to have been that of the hospital. The source of the cost data was not reported. The quantities of the resources used were obtained using actual data derived from the trial and were measured from August 1999 to August 2000. No price year was reported.

Statistical analysis of costs
Statistical analyses of the total costs were carried out to test the statistical significance of the results.

Indirect Costs
The indirect costs were not included in the analysis.
Currency
Taiwan dollars (NT$). US dollars ($) were converted into NT$ using the conversion rate of US$1 = NT$33.

Sensitivity analysis
No sensitivity analyses were carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The admission fees were NT$131,512 (+/- 83,462) in the PC group and NT$144,405 (+/- 77,821) in the PG group, (p=0.451).

The fees for the outpatient clinic visits were NT$11,296 (+/- 11,478) in the PC group and NT$13,520 (+/- 10,542) in the PG group, (p=0.341).

The fees for the emergency room visits were NT$900 (+/- 2,707) in the PC group and NT$919 (+/- 2,045) in the PG group, (p=0.969).

The fees for the chemotherapy drugs were NT$238,734 (+/- 119,755) in the PC group and NT$296,641 (+/- 135,674) in the PG group, (p=0.035).

The overall costs were NT$382,442 (+/- 168,828) in the PC group and NT$455,484 (+/- 152,218) in the PG group, (p=0.034).

The total days in or calling at the hospital were 32.9 (+/- 16.8) in the PC group and 39.1 (+/- 15.3) in the PG group, (p=0.069).

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The authors concluded that "because of the similar efficacy and good toxicity profiles of both groups, but the greater expense and length of treatment time in the paclitaxel plus gemcitabine treatment arm, paclitaxel plus carboplatin should be considered for NSCLC (non-small-cell lung cancer) patients instead of non-platinum chemotherapy with a paclitaxel plus gemcitabine regimen".

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. PC and PG were compared as their efficacy and cost-effectiveness had not been fully addressed in the literature. You should assess which chemotherapeutic regimen is currently implemented in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a phase II randomised controlled trial, which enhanced the internal validity of the analysis. In addition, the study groups were comparable at baseline and all of the patients included in the study were accounted for in the analysis. The authors noted, however, that the main health outcome was not an appropriate outcome measure. Survival would have been more appropriate, but the study was under-powered to detect statistically significant differences in terms of survival.
Validity of estimate of measure of benefit
The health outcomes were generally similar in the two study groups. Thus, no summary benefit measure was used and a cost-minimisation analysis was carried out, although the authors did not explicitly stated this. The study may also, therefore, be considered as a cost-consequences study as several health outcomes were included in the effectiveness analysis.

Validity of estimate of costs
It appears that all the categories of costs related to the chemotherapeutic treatments were included in the study. The price year was reported and currency conversions were appropriately carried out. However, the source of the cost estimates was not reported. The unit costs and the quantities of resources were not given. It was unclear whether the charges or costs were included in the analysis. These features tend to limit the internal and external validity of the cost analysis.

Other issues
The authors made some comparisons of their findings with those from other studies. The issue generalisability of the study results to other settings was not explicitly addressed and sensitivity analyses were not carried out. Thus, the relevance to other settings may be quite low. The authors enrolled a selected sample of patients with NSCLC and this was reflected in the conclusions of the study. The authors reported the results in detail and acknowledged that the study was under-powered to detect statistically significant differences in survival.

Implications of the study
The authors recommend the use of PC for the treatment of patients with NSCLC. The caveats of this finding should, however, be considered in terms of decision-making and new research in this area.

Source of funding
Supported in part by Taiwan Bristol-Myers Squibb Company, by provision of paclitaxel and carboplatin.

Bibliographic details

PubMedID
11863090

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Antineoplastic Combined Chemotherapy Protocols /adverse effects /economics /therapeutic use; Carboplatin /adverse effects /economics /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy /economics; Cost-Benefit Analysis; Deoxycytidine /adverse effects /analogs & derivatives /economics /therapeutic use; Disease Progression; Female; Humans; Lung Neoplasms /drug therapy /economics; Male; Middle Aged; Neoplasm Staging; Paclitaxel /adverse effects /economics /therapeutic use; Survival Rate; Time Factors

AccessionNumber
22002000518