Cost-minimisation analysis of three regimens of chemotherapy (docetaxel-cisplatin, paclitaxel-cisplatin, paclitaxel-carboplatin) for advanced non-small-cell lung cancer

Rubio-Terres C, Tisaire J L, Kobina S, Moyano A

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 study involved patients with advanced (stage IIIB and IV) non-small cell lung cancer (NSCLC) who were given one of three first-line chemotherapy treatments. These were:

docetaxel plus cisplatin (DOC+CIS), 75 mg/m^2 per day of each, with docetaxel given intravenously for one hour every 21 days;

paclitaxel plus cisplatin (PAC+CIS), 175 mg/m^2 per day PAC and 75 mg/m^2 per day CIS, with PAC given intravenously over either 3 or 24 hours every 21 days; and

paclitaxel plus carboplatin (PAC+CAR), 175 or 400 mg/m^2 per day PAC and 400 mg/m^2 per day CAR, with PAC given intravenously for 3 hours every 21 days.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with stage IIIB or IV NSCLC.

Setting
The setting was secondary care. The study was conducted in the USA.

Dates to which data relate
The dates during which the effectiveness evidence were gathered were not reported. However, the results of the efficacy study were presented in 2000. The calculations of hypothetical resource use were taken from publications published between 1997 and 2000. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a single published efficacy study. (See Other Publications of Related Interest).

Link between effectiveness and cost data
The cost data were derived retrospectively from the literature and, therefore, were not from the same sample used in
the effectiveness study.

**Study sample**

There were 293 patients in the DOC+CIS group, 292 patients in the PAC+CIS group and 290 patients in the PAC+CAR group. Further information on power calculations, the method of sample selection, the individuals invited to participate who refused and those excluded from the study, can be found in the effectiveness study.

**Study design**

This was a randomised, controlled multi-centre trial. The patients were randomised to one of the possible chemotherapy regimes. Further information can be found in the effectiveness study.

**Analysis of effectiveness**

The basis of the analysis was intention to treat. The primary health outcomes used were median survival time, overall time to response, and prevalence of the following toxicities:

- granulocytopenia grade 3/4,
- thrombocytopenia grade 4,
- anaemia grade 3/4,
- infections grade 3/4/5,
- febrile neutropenia grade 3/4,
- cardiotoxicity grade 3/4/5,
- renal toxicity grade 3/4/5,
- nausea grade 3 and vomiting grade 3/4,
- diarrhoea grade 3/4,
- hypersensitivity reactions grade 3/4,
- fatigue grade 3/4,
- peripheral neuropathies grade 3/4.

No data were reported to show that the patients were comparable at baseline, although these data were provided in the parent study.

**Effectiveness results**

The median survival time was 7.4 months for patients receiving DOC+CIS, 7.8 months for those receiving PAC+CIS, and 8.2 months for those receiving PAC+CAR.

The overall response rate was 17.4% for patients receiving DOC+CIS, 21.3% for those receiving PAC+CIS, and 15.3% for those receiving PAC+CAR.

The following toxicity results were reported.

- Granulocytopenia grade 3/4: 69.0% with DOC+CIS, 75.0% with PAC+CIS and 64.0% with PAC+CAR.
Thrombocytopenia grade 4: 1.0% with DOC+CIS, 2.0% with PAC+CIS and 2.0% with PAC+CAR.

Anaemia grade 3/4: 16.0% with DOC+CIS, 13.0% with PAC+CIS and 10.0% with PAC+CAR.

Infections grade 3/4/5: 9.0% with DOC+CIS, 10.0% PAC+CIS and 7.0% with PAC+CAR.

Febrile neutropenia grade 3/4: 10.0% with DOC+CIS, 16.0% with PAC+CIS and 4.0% with PAC+CAR.

Cardiotoxicity grade 3/4/5: 5.0% with DOC+CIS, 2.0% with PAC+CIS and 4.0% with PAC+CAR.

Renal toxicity grade 3/4/5: 3.0% with DOC+CIS, 3.0% with PAC+CIS and 1.0% with PAC+CAR.

Nausea grade 3 and vomiting grade 3/4: 45.0% with DOC+CIS, 49.0% with PAC+CIS, and 17.0% with PAC+CAR.

Diarrhoea grade 3/4: 10.0% with DOC+CIS, 8.0% with PAC+CIS and 2.0% with PAC+CAR.

Hypersensitivity reactions grade 3/4: 7.0% with DOC+CIS, 2.0% with PAC+CIS and 2.0% with PAC+CAR.

Fatigue grade 3/4: 17.0% with DOC+CIS, 15.0% with PAC+CIS and 14.0% with PAC+CAR.

Peripheral neuropathies grade 3/4: 5.0% with DOC+CIS, 5.0% with PAC+CIS and 10.0% with PAC+CAR.

No results were reported as being statistically significantly different.

Clinical conclusions
There were no statistically significant clinical differences between the three chemotherapy regimes.

Measure of benefits used in the economic analysis
A cost-minimisation analysis was conducted, as all three chemotherapy regimes were found to be equally effective.

Direct costs
Discounting was not carried out. This was appropriate since the duration of the treatment was less than one year, and the patients were not evaluated after that time. The quantities and the costs were analysed separately. The costs were estimated, partly using actual data from the ECOG study and several Spanish sources, and partly using hypothetical cost data from several sources that described the details of the main treatment and treatment of all the side effects. The costs measured were for the chemotherapy drugs, pre-treatment and support treatment, intravenous hydration before CIS, preparation of diluents, time in outpatients clinic, inpatient hospital stay, nursing time, medical staff time, monitoring and laboratory tests, and toxicity treatment.

The direct costs were obtained from a variety of sources in the literature. Several other sources were also used to cost the treatment for adverse drug events and toxicities. The drug prices were obtained from the Spanish Catalogue of Pharmaceutical Specialties. Other prices were taken from a database on Spanish Health Resource Costs. The price year was 2000.

Statistical analysis of costs
The standard deviation of some costs was given.

Indirect Costs
No indirect costs were included.
Currency
Spanish pesetas (Pta). The summary costs results were also given in euros and US dollars. The conversion rates were 1 euro = Pta 166.386 and $1 = Pta 186.101.

Sensitivity analysis
A sensitivity analysis was carried out. It was assessed whether the cost results were sensitive to the PAC dose in the ECOG study, as the initial cost calculations were conducted under the assumption of the dosage recommended by the manufacturer. Some of the resource use estimates were given with a standard deviation. The sensitivity analysis calculated the effect of taking the maximum and minimum value from the resource use figures.

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

Cost results
The average cost per patient was estimated as Pta 1,067,836 for DOC+CIS, Pta 1,365,304 for PAC+CIS (3-hour infusion) and Pta 1,417,995 for PAC+CAR.

The median duration of the treatment was 4 cycles, one cycle every 21 days.

The costs of the adverse effects were dealt with in the costing.

Synthesis of costs and benefits
The costs and benefits were not combined since the authors conducted a cost-minimisation analysis. The sensitivity analysis did not change the ranking of the costs of the three kinds of chemotherapy.

Authors' conclusions
Since docetaxel plus cisplatin (DOC+CIS) turned out to be the cheapest chemotherapy and was not any less effective, there is a strong argument for using it. However, the authors are aware that only one clinical trial was used for the effectiveness results. They also pointed out that the costs were derived from completely different data sources than from the effectiveness study.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was valid as it compared three well established chemotherapy regimes for NSCLC. You should determine whether these alternatives are relevant for your own setting.

Validity of estimate of measure of effectiveness
The authors carried out a systematic review of the literature in order to assess the effectiveness of the three regimes. However, they used the ECOG study as the source of the effectiveness data. The reader is referred to the ECOG study in order to assess the validity of the effectiveness result, which was that there was no significant difference between the three chemotherapy regimes.

Validity of estimate of measure of benefit
No summary estimate of benefit was used, as all three chemotherapy regimes were found to be equally effective and a cost-minimisation study was carried out. The finding of equivalent effectiveness was supported by statistical analyses.

Validity of estimate of costs
All relevant direct costs were estimated, apart from the costs of palliative care. However, the indirect costs were not calculated. The chemotherapy regimes differed in terms of how much time was spent on outpatient visits. The regimen that took the least amount of time was DOC+CIS, which also cost the least. Therefore, including the indirect costs would strengthen the argument in favour of DOC+CIS. The costs and the quantities were reported separately. Several different published sources were used for the quantities, but the authors could have presented the sources used for the different cost components more clearly.

Other issues
The authors referred to another Canadian cost-minimisation study that used the results from the ECOG 1594 trial. The latter study found that DOC+CIS was the cheapest regimen (Can$7,736). However, it also found that if the PAC+CIS regimen was administered in outpatients over 3 hours it would be even cheaper (Can$7,117). This last result differs from the one in the current study. The cost calculations used several different sources, many of them Spanish, and it was unclear whether the results were generalisable to other countries.

Implications of the study
The authors concluded that DOC+CIS is cheaper than PAC+CIS and PAC+CAR for NSCLC first-line treatment. However, they acknowledge the limitations of a study in which the costs studied were not the actual costs incurred in the trial. Therefore, a study which calculates the actual resource costs of an effectiveness trial would be very useful.

Source of funding
Supported by a research grant from Aventis Pharma SA.

Bibliographic details

PubMedID
11750717

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Carboplatin /economics; Carcinoma, Non-Small-Cell Lung /drug therapy /economics; Cisplatin /economics; Cost-Benefit Analysis; Drug Costs; Economics, Pharmaceutical; Humans; Infusions, Intravenous; Lung Neoplasms /drug therapy /economics; Neoplasm Staging; Paclitaxel /analogs & derivatives /economics; Sensitivity and Specificity; Survival Rate; Taxoids

AccessionNumber