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

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Abstract

Purpose: To compare the efficiency (the evaluation of efficacy in relation to costs) of three first-line treatment options for advanced non-small cell lung cancer (stage IIIB and IV) used in the Eastern Cooperative Oncology Group (ECOG) study: docetaxel/cisplatin (75/75 mg/m^2/day, 1 h intravenous (i.v.) infusion of docetaxel), paclitaxel/cisplatin (175/75 mg/m^2/day, 3 or 24 h i.v. infusion of paclitaxel) and paclitaxel/carboplatin (175/400 or 225/400 mg/m^2/day, 3 h i.v. infusion of paclitaxel). *Methods:* The results of the ECOG 1594 phase III clinical trial (Proc. Am. Soc. Clin. Oncol. 19 (2000) 2) demonstrated equivalent efficacy (survival, objective response) between the treatment options. To differentiate between the treatment options, we performed a cost-minimisation analysis, using a pharmacoeconomic model. *Results:* The average estimated treatment cost per patient (median, 4 cycles) with docetaxel/cisplatin would be 1 067 836 Spanish pesetas (Ptas) (6418 Euros; 5741 US dollars (USD)), 1 365 304 or 1 439 369 Ptas (8205 or 8651 Euros; 7340 or 7738 USD) with paclitaxel/cisplatin (3 or 24 h infusions, respectively), and 1 417 995 or 1 616 784 Ptas (8522 or 9717 Euros; 7623 or 8692 USD) (paclitaxel dose of 175 or 225 mg/m^2/day, respectively) with paclitaxel/carboplatin. *Conclusion:* According to our study, the treatment option docetaxel/cisplatin, with equal efficacy, would result in a cost saving of between 297 468 and 548 948 Ptas (1788 and 3299 Euros; 1599 and 2951 USD) per patient treated. This difference is mainly due to the lower treatment cost of docetaxel.

Keywords: Non-small-cell lung carcinoma; Docetaxel; Paclitaxel; Cisplatin; Carboplatin; Cost analysis

1. Introduction

In 1997 lung cancer caused 14 983 deaths in Spain [1], and in 1995 it resulted in an estimated loss of 515 potential life years in the Spanish population of between 0 and 70 years of age, of both sexes [2]. Furthermore, it is the main cause of cancer death in men aged between 45 and 54; the mortality rate in women has also increased as a result of this pathology [3]. Non-small-cell lung cancer (NSCLC) represents approximately 80% of all lung cancer cases. About 70% of all NSCLC are locally advanced or in metastatic stages (III and IV) at the time of diagnosis [4]. The median survival time of NSCLC is from 10 to 12 months in stages IIIA and IIIB and about 6 months in stage IV [5].

A meta-analysis of 11 randomised clinical trials concluded that radiotherapy combined with platinum compounds as first-line treatment reduced by 10% the risk of death by NSCLC, in comparison with radiotherapy alone [5]. In another meta-analysis of 54 randomised trials, the addition of platinum to radiotherapy resulted in a 4% increase in survival by 2 years [6]. Nevertheless, these survival benefits are less in stages IIIB and IV than in stage IIIA [7].

The present study compared efficacy and costs, i.e. the efficiency of the three combinations of taxanes and platinum agents frequently used in stage IIIB and IV NSCLC: docetaxel + cisplatin (DOC + CIS), paclitaxel + cisplatin (PAC + CIS) and paclitaxel + carbo-

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platin (PAC + CAR) [8]. The aim of this study was to determine which of the three treatment options was the most efficient first-line agent in advanced stage IIIB and IV NSCLC.

2. Methods

2.1. Pharmacoeconomic model

The study used a pharmacoeconomic model, as a theoretical outline, permitting simulations of complex health processes related to drugs. The outline follows a previously established protocol, with estimations obtained from the available or published data on efficacy, toxicity and costs of the compared options [9].

The type of pharmacoeconomic analysis applied depends on whether proven differences in efficacy exist between the treatments. As a result, an attempt was made to locate all the comparative clinical trials carried out with the three treatment options through a systematic bibliographical review in various databases (Medline, Embase, The Cochrane Library, Cancerlit) from the date the databases were created up to December 2000.

2.2. Effectiveness estimation

The systematic bibliographical review carried out identified only one randomised clinical trial, recently published by the Eastern Cooperative Oncology Group (ECOG), which compared, among others, the three treatment options analysed in the present study. The efficacy and toxicity evaluation in this study is based on the published results, the ASCO abstract and plenary presentation [10,11]. The ECOG 1594 trial objectives were to compare overall survival (primary) and response rate, time to progression and toxicities (secondary) in 1207 previously untreated patients with advanced (stage IIIB or IV) NSCLC. Table 1 indicates the treatment schedules of the options considered in the pharmacoeconomic analysis: those recommended (for second-line NSCLC in the case of taxanes) in the approved summaries of product characteristics of pharmaceutical specialities [12,13] (base case) as well as those used in the ECOG clinical trial (sensitivity analysis). A recently published study, reviewing 176 clinical trials on chemotherapy in NSCLC, revealed a statistically significant correlation between the response rate and the median survival time [14]. Nevertheless, this correlation remains an object of discussion [4]. Consequently, the effectiveness of the treatment options was evaluated in our study according to two parameters: the overall response rate and the median survival time. Toxicities of grade 3–4 of the different options were also evaluated according to the World Health Organisation (WHO) criteria [15] with the aim of establishing the costs generated by this concept in each case (Table 2).

2.3. Type of analysis

Based on the assumption that no proven differences exist in the clinical efficiency obtained with DOC + CIS, PAC + CIS and PAC + CAR, we conducted a cost-minimisation analysis (CMA) following the general

Table 1
Treatment schedules considered in the pharmacoeconomic analysis of first-line treatment of stage IIIB–IV non-small-cell lung cancer with docetaxel and cisplatin (DOC+CIS), paclitaxel and cisplatin (PAC+CIS) and paclitaxel and carboplatin (PAC+CAR)

Treatment	Dose schedule (mg/m^2/day)	Base case[a]	Sensitivity analysis[b]	Median number of administered cycles[c]
DOC+CIS	75 DOC and 75 CIS 1 h intravenous (i.v.) infusion Cycles every 21 days [10–12]	+	+	4
PAC+CIS	175 PAC and 75 CIS 3 h i.v. infusion Cycles every 21 days [12]	+		4
	175 PAC and 75 CIS 24 h i.v. infusion Cycles every 21 days [10,11]		+	4
PAC+CAR	175 PAC and 400 CAR 3 h i.v. infusion Cycles every 21 days [12]	+		4
	225 PAC and 400 CAR 3 h i.v. infusion Cycles every 21 days [10,11]		+	4

[a] The administration guidelines recommended in the summaries of product characteristics of pharmaceutical specialities were considered in the base case [12].
[b] The sensitivity analysis was performed with the doses used in the ECOG clinical trial [10,11].
[c] Median number of administered cycles estimated from ECOG trial in all cases [10,11].

Table 2
Efficacy and toxicity results of first-line treatment of stage IIIB–IV non-small-cell lung cancer with docetaxel and cisplatin (DOC+CIS), paclitaxel and cisplatin (PAC+CIS) and paclitaxel and carboplatin (PAC+CAR) [10,11]

Item[a]	DOC+CIS ($n=293$[b])	PAC+CIS ($n=292$)	PAC+CAR ($n=290$)
Efficacy			
Median survival time	7.4	7.8	8.2
Survival after 1 year	31	31	35
Median time to progression	3.6	3.5	3.3
Objective response			
Complete (CR)	0.4	0.3	0.3
Partial (PR)	17	21	15
Overall (CR+PR)	17.4	21.3	15.3
Haematologic toxicities			
Granulocytopaenia grade 3/4	69.0	75.0	64.0
Thrombocytopaenia grade 4	1.0	2.0	2.0
Anaemia grade 3/4	16.0	13.0	10.0
Non-haematologic toxicities			
Infections grade 3/4/5[c]	9.0	10.0	7.0
Febrile neutropaenia grade 3/4	10.0	16.0	4.0
Cardiotoxicity grade 3/4/5[c]	5.0	2.0	4.0
Renal toxicity grade 3/4/5[c]	3.0	3.0	1.0
Nausea grade 3 and vomiting grade 3/4	45.0	49.0	17.0
Diarrhoea grade 3/4	10.0	8.0	2.0
Hypersensitivity reactions grade 3/4	7.0	2.0	2.0
Fatigue grade 3/4	17.0	15.0	14.0
Peripheral neuropathies grade 3/4	5.0	5.0	10.0

[a] Percentage in all cases, except in median survival and median time to progression (months).
[b] Number of patients evaluated.
[c] Costs of patients with grade 5 toxicities occurring before death.

guidelines for pharmacoeconomic analyses in Spain [16] and the specific guidelines for CMA published by the Canadian Coordinating Office for Health Technology Assessment [17] and Butler University [18]. Published NSCLC pharmacoeconomic analyses [19–22] were used to build the model.

2.4. Study perspective

In Spain, the antineoplastic agents studied are for hospital use (CIS, DOC, PAC) or for hospital diagnosis (CAR), and in practice are for intrahospital use, the cost of which are fully covered by the Spanish National Health Service (NHS) [13]. For this reason, the present study was carried out from the hospital perspective of the NHS.

2.5. Time horizon

It was not necessary to apply any discount to future costs or benefits, as the comparison was limited to the duration of the complete treatment. This was less than 1 year, according to the median of the number of cycles administrated in the ECOG study [10,11] (which was 4 cycles; one cycle every 21 days, for the three options) (Table 1).

2.6. Cost estimation

The estimated cost of a disease treated with a specific drug is calculated by identifying and quantifying the health resources involved and assigning them specific unit costs. In this way, the average costs were estimated for a typical patient with NSCLC receiving treatment with DOC + CIS, PAC + CIS or PAC + CAR. The costs of the health resources used in the model are from the year 2000 and are presented in Spanish pesetas (Ptas), in Euros (1 Euro = 166.386 Ptas) and in US dollars (1 USD = 186.010 Ptas). The costs evaluated were those pertaining to the acquisition of the drug from its origin, hospital stays, premedication regimen/diluents and the time employed by the required nursing and medical staff for the drug administration and the necessary monitoring costs prior, during and between cycles. Costs incurred by adverse reactions associated with the different treatment options were also estimated.

2.6.1. Health resources

The type and quantity of health resources utilised was estimated mainly from the bibliography on Spanish clinical practice in the treatment of NSCLC. The health resources utilised for a typical patient with NSCLC treated with each option are outlined in Table 3.

Table 3
Estimate of resources utilised (apart from antineoplastic) for a typical patient with NSCLC, during one chemotherapy cycle[a]

Resource	DOC+CIS	PAC+CIS	PAC+CAR
Pretreatment and support treatment[a] [12,13]	Dexamethasone (44 mg, p.o.) Ondansetron (40 mg, i.v.)	Dexamethasone (44 mg, p.o.) Dexchlorpheniramine (5 mg, i.v.) or diphenhydramine (50 mg, p.o.) Cimetidine (300 mg, i.v.) or ranitidine (50 mg, i.v.) Ondansetron (40 mg, i.v.)	Dexamethasone (44 mg, p.o.) Dexchlorpheniramine (5 mg, i.v.) or diphenhydramine (50 mg, p.o.) Cimetidine (300 mg, i.v.) or ranitidine (50 mg, i.v.) Ondansetron (40 mg, i.v.)
Intravenous hydration before CIS [12,13]	Glucose saline serum (500 ml) KCl (3 g in 500 ml) Mannitol 10% (500 ml)	Glucose saline serum (500 ml) KCl (3 g in 500 ml) Mannitol 10% (500 ml)	Glucose saline serum (500 ml) KCl (3 g in 500 ml) Mannitol 10% (500 ml)
Diluents (preparation) [12,13]	Dilute with solution of NaCl at 0.9% (1250 ml)	Dilute with solution of NaCl at 0.9% (1250 ml)	Dilute with solution of NaCl at 0.9% (1250 ml)
Time in outpatients' clinic (h) [12,13]	12.5[b] (1 h i.v. infusion of DOC)	14.5[b] (3 h i.v. infusion of PAC) or 35.5[b] (24 h i.v. infusion of PAC)	7.5 (3 h i.v. infusion of PAC)
Nursing time [24]	It is estimated that the nurse requires, for each treatment, 3 min for preparation, 2 min for stabilisation and 1 min for surveillance for every 15 min of infusion	It is estimated that the nurse requires, for each treatment, 3 min for preparation, 2 min for stabilisation and 1 min for surveillance for every 15 min of infusion	It is estimated that the nurse requires, for each treatment, 3 min for preparation, 2 min for stabilisation and 1 min for surveillance for every 15 min of infusion
Medical staff time [25]	It is estimated as 10 min daily attention per patient	It is estimated as 10 min daily attention per patient	It is estimated as 10 min daily attention per patient
Monitoring and laboratory tests (excluding those of CIS or CAR) [12,13]	One physical examination every 3 months, one chest radiography, complete haemogram (one prior to cycle, one intermediate) and hepatic function test (one prior to cycle)	One physical examination every 3 months, one chest radiography, complete haemogram (one prior to cycle, one intermediate), electrocardiogram (one basal) and hepatic function test (one prior to cycle)	One physical examination every 3 months, one chest radiography, complete haemogram (one prior to cycle, one intermediate), electrocardiogram (one basal) and hepatic function test (one prior to cycle)
Toxicity treatment	See text	See text	See text

[a] Total doses per cycle in all cases.
[b] Time of admittance/administration: 3.5 h pretreatment; 8 h CIS; 1 h CAR.

The costs of premedication, the required hydration for CIS and the diluents used were estimated from clinical practice in Spain, as well as the recommendations in the summaries of product characteristics of pharmaceutical specialities (for second-line NSCLC in the taxanes case) [12,13]. The length of the outpatients' hospital stay was estimated from the duration of the intravenous infusion of each treatment, determined in the case of DOC and PAC by the recommendations in the summaries of product characteristics, and considering that 3.5 h are needed for pretreatment, 8 h for CIS administration and 1 h for CAR administration (Table 3). To break up the nursing costs and those of the laboratory and diagnostic tests, these were excluded from the hotel cost of the hospital stay. According to the results of the Cost per Process Project of the Spanish National Institute of Health (INSALUD), carried out in 29 Spanish hospitals, the costs per medical staff and drugs made up 25% of the total hospitalisation cost [23]. With the aim of avoiding duplicate costs as such, only those costs pertaining to non-medical staff, maintenance, supplies and other costs, such as depreciation of the hospital building, were taken into consideration; all of them estimated at 75% of the cost per outpatient hospital stay. The medical costs were calculated separately as those of the medical and nursing staff and the acquisition of pharmaceutical products.

Storage cost of the agents (at room temperature) were not considered because they are difficult to calculate and of minimal impact [24].

For each cycle, it was estimated that a nurse would require 3 min for the preparation of the drug, 2 min for establishment and 1 min surveillance for every 15 min of infusion [24]. To calculate the nursing costs, the number of nursing hours was multiplied by the estimated average salary of a NHS nurse [25]. The medical staff costs were calculated by estimating the time of attention dedicated to each patient in the outpatients hospital as 10 min per day [25]. The types and quantities of monitoring and laboratory tests were taken from the summaries of product characteristics of the treatment options compared [12,13].

The costs incurred by drug adverse events (DAE) were calculated by multiplying the DAE treatment cost by its appearance probability, taken from the results of the ECOG study [10,11] (Table 2). In cases of haematologic toxicity, certain treatments were assumed. For febrile neutropaenia, cost was based on the empiric administration of an antibiotic combination (2 g intravenous (i.v.) ceftazidime every 8 h and 500 mg amikacin every 12 h) for an average of 7 days and the hospitalisation of a patient for 5 days in the Oncology Unit [26]. For granulocytopaenia of grade 3–4 of the WHO criteria, cost was based on treatment with a haematopoietic growth factor (G-CSF) (300 μg/day filgrastim for 4 days) [26,27]. For thrombocytopaenia of grade 4 of the WHO criteria, cost was based on treatment, on average, with two platelet concentrates for every 10 kg weight [28]. The cost of treating patients with grade 3–4 anaemia was based on the administration of an average of 3 U red blood cell concentrate [29].

In the case of non-haematologic toxicities (grade 3–5 of the WHO criteria), the cost of infections was estimated by considering the average value [21] of the antimicrobial treatments for pneumonia in patients with comorbidity, acute pyelonephritis and septicaemia (2 g i.v. cefotaxim, every 8, 8 and 6 h, respectively, for 7 days) [30]. Likewise, it was estimated that patients would receive i.v. antimicrobial treatment in hospital during a period of 7 days [10,11]. The cost of a case of cardiotoxicity was calculated by establishing that a patient should be hospitalised for 6 days [31]. Finally, it was estimated that a patient with renal toxicity (DRG 316) would be hospitalised for 9 days on average [21,25].

The costs of other non-haematologic toxicities (grade 3–4 of the WHO criteria) were calculated as follows. Vomiting would be treated with ondansetron [32] (8 mg/12 h, for 5 days [13]), and diarrhoea with solutions of oral rehydration (2 l daily of glucose and electrolytes) and loperamide (10 mg/day, for 2 days) [33]. In cases of hypersensitivity, an antihistamine like diphenhydramine would be orally administered (25–50 mg, four times per day) [33]. Finally, the recommended treatment for chemotherapy-induced peripheral neuropathies would involve the daily oral administration of 25 mg nortriptyline for a period of 3 weeks [34].

Downstream costs, such as palliative care, were not taken into account as no published data on this issue are available in the Schiller et al. study [10,11].

2.6.2. Unit costs

The unit costs used in the pharmacoeconomic analysis are shown in Table 4. The acquisition costs of the drugs, diluents and serums were obtained from the Spanish Catalogue of Pharmaceutical Specialties 2000 [13]. The remaining health resources unit costs were estimated from a database on Spanish Health Resource Costs [25].

2.7. Sensitivity analysis

A simple one-way sensitivity analysis was performed to test the robustness of the results in the base case [35]. The analysis included the minimum and maximum values of the costs of the hospital stays and diagnostic and laboratory tests from the standard deviations of the base case average values (Table 4). The effects of paclitaxel dosage and administration were also considered according to the patterns used in the ECOG study [10,11] rather than those recommended in the autho-

Table 4
Unit costs utilised in the comparative pharmacoeconomic analysis of docetaxel and cisplatin (DOC+CIS), paclitaxel and cisplatin (PAC+CIS) and paclitaxel and carboplatin (PAC+CAR) in the first-line treatment of stage IIIB–IV non-small-cell lung cancer

Resource (number, type)	Unit cost (Ptas) (S.D.)	Reference
Docetaxel (1 vial of 80 mg)[a]	94 864	[13]
Docetaxel (1 vial of 20 mg)[a]	24 255	[13]
Paclitaxel (1 vial of 100 mg)[a]	70 997	[13]
Paclitaxel (1 vial of 30 mg)[a]	21 299	[13]
Cisplatin (1 vial of 50 mg)[a]	3816	[13]
Cisplatin (1 vial of 10 mg)[a]	767	[13]
Carboplatin (1 vial of 450 mg)[a]	28 735	[13]
Carboplatin (1 vial of 150 mg)[a]	9049	[13]
Carboplatin (1 vial of 50 mg)[a]	3292	[13]
Dexamethasone (3 vials of 4 mg)[a]	371	[13]
Ondansetron (50 vials of 8 mg)[a]	108 171	[13]
Dexchlorpheniramine (5 vials of 5 mg)[a]	265	[13]
Diphenhydramine (25 capsules of 25 mg)[a]	234	[13]
Diphenhydramine (25 capsules of 50 mg)[a]	261	[13]
Cimetidine (10 vials of 200 mg)[a]	724	[13]
Ranitidine (100 vials of 50 mg)[a]	4695	[13]
Filgrastim (5 syringes of 300 μg)[a]	80 579	[13]
Cefotaxime (100 vials of 1 g)[a]	94 509	[13]
Ceftazidime (50 vials of 2 g)[a]	142 890	[13]
Amikacin (50 vials of 500 mg)[a]	32 218	[13]
Loperamide (20 capsules of 2 mg)[a]	823	[13]
Methylphenidate (30 tablets of 10 mg)[a]	564	[13]
Nortriptyline (500 tablets of 25 mg)[a]	4499	[13]
Oral rehydration (solution of 500 ml)[a]	355	[13]
Red blood cells concentrate (one)	10 036	[25]
Platelet concentrate (one)	7806	[25]
Glucose saline solution (10 bottles of 500 ml)[a]	2292	[13]
CIN serum at 0.9% (50 bottles of 50 ml)[a]	8682	[13]
CIN serum at 0.9% (20 bottles of 250 ml)[a]	4322	[13]
CIN serum at 0.9% (10 bottles of 1.000 ml)[a]	2705	[13]
Potassium chloride (100 bottles of 3g)[a]	17 224	[13]
Mannitol 10% (20 bottles of 250 ml)[a]	5461	[13]
Outpatients hospital/Oncology (1 day)	28 215 (3896)	[25]
Hospital stay Oncology (1 day)	45 888 (8192)	[25]
Hospital IV transfusion (one)	14 036 (3093)	[25]
Average nurse's fee (1 h)	2340	[25]
Average doctor's fee (1 h)	2820	[25]
Physical examination/external visit (one)	12 271 (4021)	[25]
Chest radiography (one)	2687 (984)	[25]
Electrocardiogram (one)	2978 (932)	[25]
Electromyography (one)	16 770 (9993)	[25]
Audiometer (one)	13 741 (10 843)	[25]
Complete haemogram (one)	1780 (367)	[25]
Determination of serum creatinine (one)	347 (271)	[25]
Determination of BUN (one)	160 (0)	[25]
Creatinine clearance (one)	942 (620)	[25]
Plasma levels of Mg, K and Ca (one)	1993 (771)	[25]
Hepatic function test (one)	1842 (0)	[25]

[a] Ex-factory sale price.

rised summary of product characteristics of the pharmaceutical speciality (base case) (Table 1).

3. Results

3.1. Base case

3.1.1. Efficacy and toxicity estimation

Table 2 summarises the ECOG clinical trial results [10,11]. There were no statistically significant differences in the overall response observed between DOC + CIS (17.4%), PAC + CIS (21.3%) and PAC + CAR (15.3%). Neither were there significant differences in the median survival time observed with the three treatment options (7.4, 7.8 and 8.2 months, respectively).

In terms of toxicities of WHO criteria grade 3–4, the highest frequency of febrile neutropaenia was seen with PAC + CIS (16%), compared with 10% with DOC + CIS and 4% with PAC + CAR. Diarrhoea and hypersensitivity reactions were observed more often with DOC + CIS (10 and 7%, respectively) than with PAC + CIS (8 and 2%, respectively) and PAC + CAR (2 and 2%, respectively). Finally, there was a lower incidence of nausea and vomiting with PAC + CAR (17%) compared with the cisplatin combinations (45% with DOC + CIS and 49% with PAC + CIS) (Table 2).

3.1.2. Cost-minimisation analysis

Table 5 outlines the base case estimated costs of a complete treatment per patient. The average estimated cost per patient of treatment (four-cycle median) would be 1 067 836 Ptas (6418 Euros; 5741 USD) for DOC + CIS, 1 365 304 Ptas (8205 Euros; 7340 USD) for PAC + CIS (3 h infusion) and 1 417 995 Ptas (8522 Euros; 7623 USD) (paclitaxel dose of 175 mg/m^2/day) for PAC + CAR. Therefore, DOC + CIS would result in a cost saving of 297 468 and 350 159 Ptas (1788 and 2104 Euros; 1599 and 1882 USD), respectively.

3.2. Sensitivity analysis

The base case results were not sensitive to the inclusion of the minimum and maximum costs of the hospital stays or diagnostic and laboratory tests, based on the standard deviations of the average values used in the base case. The cost saving with DOC + CIS would range between 291 676 and 350 875 Ptas (1753 and 2109 Euros; 1568 and 1886 USD) (Table 5). Considering the dosage used in the ECOG study [10,11], the saving with DOC + CIS would be higher, between 371 533 and 548 948 Ptas (2233 and 3299 Euros; 1997 and 2951 USD) (Table 6).

These differences are mainly due to the treatment cost of PAC + CIS and PAC + CAR; 29 and 38% more expensive than DOC + CIS, respectively. Likewise, the

Table 5
Average cost estimates per patient of first-line treatment of stage IIIB–IV non-small-cell lung cancer with docetaxel+cisplatin (DOC+CIS), paclitaxel+cisplatin and paclitaxel+carboplatin[a]

Item	Base case (Ptas)	Minimum costs (Ptas)	Maximum costs (Ptas)
Docetaxel+cisplatin			
Acquisition of the drugs from origin	610 160	610 160	610 160
Premedication and diluents	54 446	54 446	54 446
Hospital stays	44 086	37 998	50 173
Nursing/medical staff time	12 105	12 105	12 105
Monitoring and laboratory tests	93 407	49 152	137 662
Toxicity	253 632	228 155	279 109
Total	1 067 836	992 016	1 143 656
Paclitaxel+cisplatin			
Acquisition of the drugs from origin	860 228	860 228	860 228
Premedication and diluents	57 804	57 804	57 804
Hospital stays	51 140	44 078	58 201
Nursing/medical staff time	26 573	26 573	26 573
Monitoring and laboratory tests	107 226	58 120	156 333
Toxicity	262 333	236 889	287 777
Total	1 365 304	1 283 692	1 446 916
Difference with DOC+CIS	297 468[b]	291 676[b]	303 261[b]
Paclitaxel+carboplatin			
Acquisition of the drugs from origin	987 873	987 873	987 873
Premedication and diluents	57 804	57 804	57 804
Hospital stays	26 452	22 799	30 104
Nursing/medical staff time	8960	8960	8960
Monitoring and laboratory tests	107 226	58 120	156 333
Toxicity	229 681	205 904	253 458
Total	1 417 995	1 341 459	1 494 531
Difference with DOC+CIS	350 159[b]	349 443[b]	350 875[b]

[a] Base case and sensitivity analysis performed with minimum and maximum unit costs.
[b] In all cases, the amount indicates the lower cost of the treatment option DOC+CIS.

treatment costs of PAC + CIS and PAC + CAR are 63 and 70%, respectively, of the total cost of the treatment, while in the case of DOC + CIS it only constitutes 57%.

4. Discussion

According to the ECOG study results, the combination of DOC + CIS is of similar efficacy to PAC + CIS and PAC + CAR in the first-line treatment of advanced NSCLC. On the other hand, the total cost of patients treated with DOC + CIS is lower than that of the paclitaxel combinations, an important factor when choosing equally effective treatment regimens.

A number of limitations in the study must be taken into account when evaluating these results. The first point is that there is only one available clinical trial that directly compares these treatment options [10,11]. On the other hand, the utilisation of resources was not estimated from a pharmacoeconomic clinical trial [35], but from clinical practice and a systematic review of the Spanish published data.

In an attempt to minimise these limitations, a sensitivity analysis was performed, increasing and decreasing the average costs of various health resources by the values corresponding to their standard deviations. How the treatment option is administered was also considered: according to the guidelines recommended in the summary of product characteristics for second-line treatment [12,13] and versus the treatment schedules used in the ECOG study [10,11]. In both cases, small quantitative variations occurred that did not affect the significance of the base case results.

Table 6
Sensitivity analysis performed comparing the recommended dosage in the summaries of product characteristics of pharmaceutical specialities (base case) [12] or those used in the ECOG study [10,11][a]

Treatment	Recommended dose (base case) [12] (Ptas)	Dose used by the ECOG [10,11] (Ptas)
PAC+CIS	297 468[b]	371 533[b]
PAC+CAR	350 159[b]	548 948[b]

[a] Estimates of the difference between the average costs per patient of treatment with docetaxel+cisplatin (DOC+CIS) and those of paclitaxel+cisplatin (PAC+CIS) or paclitaxel+carboplatin (PAC+CAR).
[b] In all cases, the amount indicates the lower cost of the treatment option DOC+CIS.

A recently published abstract of a Canadian cost-minimisation analysis used, as in our study, the efficacy data of the ECOG 1594 trial. According to this study, in the Canadian environment, DOC + CIS would be the least costly of the three regimens with taxanes evaluated in the ECOG trial, the total treatment costs for DOC + CIS being 7736 Can$, for PAC + CIS being 8318 Can$, and for PAC + CAR being 8414 Can$. However, according to this study, PAC + CIS would be competitive (7117 Can$) if administered over a shorter duration (3 h infusion) in an outpatient setting [36]. The significance of these results coincides with ours, except that in our analysis the 3 h infusion of PAC + CIS would be more expensive than that of DOC + CIS. It is not possible to analyse the reason for this discrepancy due to the lack of data available in the Canadian study.

5. Conclusion

According to the results of our study, NSCLC first-line treatment with docetaxel and cisplatin, although equally effective as PAC + CIS and PAC + CAR, would result in a cost saving ranging between 297 468 and 548 948 Ptas (1788 and 3299 Euros; 1599 and 2951 USD) per patient treated. This difference is mainly due to the lower treatment cost of docetaxel compared with paclitaxel.

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