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Economic Analysis of Carboplatin Versus Cisplatin in Lung and Ovarian Cancer

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Abstract

Objective: To conduct an economic analysis on the use of carboplatin versus cisplatin over multiple courses in patients with lung [nonsmall cell lung cancer (NSCLC) and small cell lung cancer (SCLC)] or ovarian cancer.

Design: This 1-year study was a prospective, multicentre, cost-minimisation evaluation. Direct medical resource utilisation and costs associated with carboplatin and cisplatin administration over 3 to 6 courses of treatment were measured and compared. The perspective of this evaluation was that of the payer.

Setting: A convenience sample of 16 sites representing a mix of cancer centres, outpatient clinics, medical centres and managed-care sites in a general practice oncology setting participated.

Patients and interventions: Patients were included in this study if they were newly diagnosed with NSCLC, SCLC or ovarian cancer, had not received prior chemotherapy, received either carboplatin or cisplatin as their treatment (additional chemotherapy agents were allowed), and received at least 3 courses of carboplatin or cisplatin therapy up to a maximum of 6 courses. Patients receiving more than 6 courses of therapy were included in this study, but data collection on those patients stopped after the sixth course.

Individuals involved with data collection at all sites were trained via on-site and/or teleconference training. Site visits were made to assure reliability of at least 0.80. Data were collected and compiled via a fax transmission process that scans directly through optical mark and character recognition into a computer database. Outcome measures included costs of: medications, emergency room visits, physician/clinic/laboratory visits, home healthcare visits, transfusions, special procedures, consultations, hospitalisations and other/miscellaneous costs.

Main outcome measures and results: Of 220 patients, 164 met the study criteria (response rate = 74.2%) with 95 patients in the carboplatin group (NSCLC = 45, SCLC = 18, ovarian = 32) and 69 in the cisplatin group (NSCLC = 36, SCLC = 21, ovarian = 12). The average number of courses were: NSCLC = 4.3 and 4.2, SCLC = 4.3 and 4.8, and ovarian = 4.7 and 5.1, respectively, for carboplatin and cisplatin. The total costs (treatment and toxicity) associated with the use of carboplatin were higher in NSCLC, similar in SCLC but lower in ovarian cancer.

Conclusions: These results indicate that overall treatment costs may vary depending on cancer type, even when the same drugs are used. The total costs (treatment plus toxicity costs) associated with the use of carboplatin were higher

than those of cisplatin in patients with NSCLC, similar in SCLC, but lower in ovarian cancer.

Cancer, following heart disease, is the second leading cause of death in the US. 'One out of every 4 deaths in the US is from cancer.'[1] As the baby boomers age, the number of patients with cancer will continue to increase. This will continue to make cancer a major health and economic concern in the US.

Lung cancer is the most common cancer in the US. According to the American Cancer Society, the estimated incidence was 171 500 new cases in 1998.[1] Lung cancer is also the most lethal cancer in the US, responsible for approximately 160 100 deaths (28% of all cancer deaths) in 1998.[1] The 5-year relative survival rate is only 14% in all patients regardless of stage.[1] Only a small percentage of patients have localised disease at the time of detection which makes chemotherapy the primary treatment of this systemic disease. However, chemotherapy has been shown to only marginally improve survival; although it does palliate symptoms and may improve quality of life.[2]

According to the American Cancer Society, ovarian cancer accounts for approximately 4% of all cancers among women in the US. They estimated 25 400 new cases and 14 500 deaths in 1998.[1] Although this cancer ranks second in incidence among gynaecological cancers, it causes the most deaths among the female reproductive organ cancers according to the American Cancer Society. The 5-year survival rate is 46%.[1] However, at the time of diagnosis, only 24% of the patients have localised disease which, again, leads to chemotherapy as the primary treatment option.

As cancer incidences continue to increase, the expenses associated with cancer care also will continue to increase. As payers continue to demand improved services and patient outcomes while scrutinising healthcare costs, the pressure to provide quality, low cost care escalates.[3] With various chemotherapy regimens available for the multitude of cancers diagnosed, it is important to select the most cost-effective agents for treatment, keeping in mind the patient's quality of life.

Current practice standards for the treatment of lung and ovarian cancer include both cisplatin and carboplatin administration. The FDA-approved indication for carboplatin is initial and secondary treatment of advanced ovarian carcinoma, while cisplatin is approved for metastatic testicular cancer, metastatic ovarian cancer and advanced bladder cancer.[4] Although not FDA-approved for lung cancer, both agents are commonly used and accepted as standard treatment for this cancer.[5] Common regimens for nonsmall cell lung cancer (NSCLC) include carboplatin plus paclitaxel, carboplatin plus etoposide, cisplatin plus etoposide, cisplatin plus gemcitabine, cisplatin plus paclitaxel, cisplatin plus vinorelbine, topotecan, and vinorelbine.[5] For small cell lung cancer (SCLC), these regimens include carboplatin plus etoposide, cisplatin plus etoposide, cyclophosphamide plus doxorubicin plus etoposide, cyclophosphamide plus doxorubicin plus vincristine, etoposide, and topotecan.[5] For ovarian cancer, the regimens include carboplatin plus cyclophosphamide, carboplatin plus paclitaxel, cisplatin plus cyclophosphamide, cisplatin plus paclitaxel, altretamine, etoposide, liposomal doxorubicin, paclitaxel, and topotecan.[5]

Studies[6-8] have shown that carboplatin and cisplatin produce equivalent clinical effects with respect to complete and partial response rates, response duration and survival for some tumour types (ovarian cancer). However, toxicities with these 2 agents are different. Although the actual drug cost of carboplatin is more expensive than cisplatin, the overall treatment and toxicity-related costs for multiple courses may be less for carboplatin than cisplatin.

Only 3 studies, Alberts,[9] Calvert and Urie,[10] and George et al.[11] have focused on the use and costs of carboplatin versus cisplatin in ovarian cancer. No studies were found that compared these drugs in lung cancer. The study conducted by Alberts[9] was the only study to have examined the toxicity-related costs in ovarian cancer over sev-

eral courses of therapy. In this study, retrospective data from a clinical trial were collected and results showed that over time, the total toxicity-related costs for 6 cycles of chemotherapy with carboplatin was $US1808[12] less than with cisplatin (combination therapy with cyclophosphamide plus cisplatin or carboplatin). Even after accounting for initial drug costs, the total savings of $US554 favored carboplatin. Average wholesale price (AWP) was determined from the 1992 Redbook and hospitalisation charge data were based upon analysis of the Medicare Medical Claims Database (MEDPAR).[12]

Alberts[9] and Calvert and Urie[10] stated that the overall costs were lower for carboplatin while George et al.[11] stated that the overall costs were similar. However, Calvert and Urie[10] estimated the costs of carboplatin and cisplatin in the treatment of only 4 patients. In addition, patients were treated per study protocol in all 3 studies. In a real world everyday treatment setting, research protocols are typically not followed in detail. Due to the difference in the results of the 3 studies, absence of data in an everyday treatment setting, and lack of prospective data (George et al.[11] used prospective data while Albert[9], and Calvert and Urie[10] used retrospective data), economic analyses in lung and ovarian cancer, prospective economic research is needed with carboplatin and cisplatin therapy in the treatment of lung and ovarian cancer.

The purpose of this study was to conduct an economic analysis on the use of carboplatin versus cisplatin over multiple courses for the following 3 disease states: (i) NSCLC; (ii) SCLC; and (iii) ovarian cancer in a general practice setting. The specific objective of this study was to measure and compare direct medical costs associated with carboplatin and cisplatin administration over a minimum of 3 to a maximum of 6 courses of treatment.

This study is similar to the study by Alberts,[9] but the data were not obtained from a protocol-driven clinical trial and other variables besides hospitalisations were examined. This study looked at not only ovarian cancer, but also lung cancer prospectively in real world settings where there are no study protocols and patients are treated as they normally would be treated by their physicians. A question that is commonly asked today by healthcare providers is 'what does it cost to treat a patient?' As third parties increase prospective prices and capitalisation agreements, this question becomes more important. The problem is that current

Table I. Treatment resource variables[a]

Resource variable component	Description
Clinic visits	A visit made to the clinic/office for a scheduled course of cancer therapy
Hospitalisation days	The difference between date admitted to and date discharged from the hospital for a scheduled course of cancer therapy
Audiograms	Whether or not an audiogram was conducted
Measurement of creatinine clearance	Whether or not creatinine clearance was measured
Consultations	Whether or not the patient received specialty consultations, e.g. nephrology, neurology, etc.
Other procedures	Any other procedures performed
Radiation therapy	Whether or not concurrent or related radiation therapy was provided
Chemotherapy agents	Name, dose, route, schedule and total number of doses of chemotherapy agents administered
Supportive agents	Name, dose, route, schedule and total number of doses of supportive agents (e.g. antiemetic therapy) administered
Additional support agents - magnesium, mannitol, potassium, diuretics	Whether or not the patient received these agents as an additive
Other additional support agents	Whether or not the patient received other additives such as intravenous fluids
Growth factors	Name, dose, number of days the treatment was given for and the total number of doses of growth factors administered

a Variables associated with any procedures, drug therapy, etc., for any of the cancer types during each course of cancer therapy.

Table II. Toxicity-management resource variables[a]

Resource variable component	Description
Clinic visits	Number of visits made to the clinic/office for a visit other than for the scheduled course of cancer therapy
Hospitalisation days	The difference between the date admitted to and date discharged from the hospital other than for the scheduled course of cancer therapy (possible to have multiple admissions)
Laboratory visits	Number of laboratory visits and the various tests performed
Emergency room visits	Number of emergency room visits
Consultations	Number of consultations
All toxicity-related procedures	Number of any toxicity-related procedures
Home healthcare	
days	Number of days the patient was visited by a home care organisation
IV fluids	Whether or not the patient received IV fluids as part of the home care treatment
antibacterials	Whether or not the patient received any antibacterials as part of the home care treatment
other	Whether or not any other therapy was given as part of the home care treatment
Transfusions	Whether or not the patient received any blood transfusions along with the total number of units received
Toxicity management agents	Name, dose, route, schedule and total number of doses of any drug given for any adverse event

a Variables associated with any procedures, drug therapy, etc., due to toxicity of the drug or the cancer type itself and performed between each scheduled course of cancer therapy.

IV = intravenous.

data systems usually do not capture all resource utilisation data needed to determine total costs. Therefore, for this study, a unique data-coding process was created to capture the information needed; including information about inpatient, outpatient and home care services over a 3- to 6-month period.

Methodology

Study Design

This study was a prospective, multicentre, cost-minimisation evaluation. The perspective was that of the payer.

An outcome and cost analysis of carboplatin and cisplatin was conducted to determine which treatment is less costly or has a potential for cost savings over time. A sensitivity analysis was carried out using 2 different estimates for costs. Although the 1996 Physicians' Fee Reference (PFR)[13] cost estimates are reported in this article, the cost estimates from the 1996 Medicare Claims Database[14] yielded similar results. Discounting was not needed because the data collection period did not exceed 1 year.

Site Selection

A convenience sample of sites representing a mix of cancer centres, outpatient clinics, managed-care sites and medical centres/private hospitals were selected. The sites were selected based on the expected number of patients being treated for lung and ovarian cancer. These sites were also selected to represent different areas of the country and different types of healthcare settings. Therefore, the sample (sites) was not selected by a random process.

30 sites were contacted and 23 sites agreed to participate. However, 7 of the 23 sites dropped out of the study due to lack of time, lack of staff, mergers, change in management and lack of response from the site coordinator. Also, some sites already had other clinical trials ongoing that would conflict with this study. The remaining 16 sites used both carboplatin and cisplatin and 12 of the 16 sites had patients in all 3 cancer diagnosis groups.

Training/Education

Before the data collection process began, the designated coordinator from each site attended a centralised training meeting. An implementation packet was created by the investigators and pro-

Table III. Medicare and physicians' fee reference tabulated and/or complied costs per event ($US; 1996 values) for various components of resource variables in the study

Resource variable component	Medicare[a]	Physicians' fee reference[b]
Arterial blood gases	27.44	78.00
Aid [prolonged services requiring direct patient contact (per h)]	90.44	128.00
Audiograms (tympanometry)	21.75	37.00
Blood count	3.36	13.00
Blood culture	14.40	50.00
Bone scan	516.00	516.00
Bronchoscopy	247.55	652.00
Catheter (angiocatheter)	27.17	61.00
CBC (diff)	8.40	24.00
Chest tube	73.00	73.00
Chest x-ray	47.51	142.00
Consultation	141.80	221.00
CT – brain	46.71	605.00
Digoxin level measurement	18.85	57.00
Doppler flow scan	67.44	219.00
Electrocardiogram	29.92	71.00
Emergency room visits	102.18	175.00
Groshong (catheter implanted in the skin for chronic chemotherapy infusion)	271.55	271.00
Home healthcare visits	64.02	87.00
Homemaker	91.80	91.80
Hospitalisation [no. of overnight stays (length of stay × cost per night)]	117.48	175.00
Laboratory visits	15.69	58.00
Magnetic resonance imaging	513.00	1031.00
MD/clinic visits	52.30	87.00
Measured creatinine clearance	13.41	49.00
Medications	AWP	AWP
Mediport (catheter implanted in the skin for chronic chemotherapy infusion)	322.50	430.00
MUGA scan (heart scan that determines the amount of blood pumped by the heart chambers)	516.00	516.00
Oxygen	21.91	95.00
Platelet measurement	6.10	22.00
Pneumonectomy	1318.22	3339.00
Pulmonary function test	40.27	103.00
Radiation therapy	115.37	420.00
Shoulder x-ray	22.18	86.00
Sputum culture	10.97	36.00
Stool sample	3.59	15.00
Thoracentesis	90.99	244.00
Transfusion: RBC & platelets/unit	39.38	68.00
Urinalysis	4.49	18.00
Ultrasound	50.30	193.00
Urine culture	9.18	30.00
WBC	5.27	19.00

a 1996 Medicare Claims Database[14].

b 75th percentile of the 1996 Physicians' Fee Reference (PFR)[13] based on 1996 Current Procedural Terminology (CPT) codes.

AWP = average wholesale price; **CBC (diff)** = differential complete blood count; **CT** = computerised tomography; **MD** = medical doctor; **MUGA** = multiple-gated arteriography; **RBC** = red blood cell count; **WBC** = white blood cell count.

vided to the coordinators for on-site use. This packet contained the programme goals, method of data collection, instruction sheets and the data collection instrument, timeline and contact person for trouble-shooting. The designated coordinators were responsible for providing on-site local training at their own institutions and obtaining Institutional Review Board (IRB) approvals.

In addition to the on-site local training, the investigators conducted additional teleconferences as needed throughout the study. Data collection began in October 1995 and ended in October 1996. For additional details of the data collection process, the reader is referred elsewhere.[15]

Patient Enrolment Criteria

Each site was asked to concurrently monitor 15 to 25 newly treated patients with NSCLC, SCLC and/or ovarian cancer.

Inclusion Criteria

Patients were included in this study if they:

- were newly diagnosed with NSCLC, SCLC or ovarian cancer
- had not received prior chemotherapy
- received either carboplatin or cisplatin as their treatment (additional chemotherapy agents were allowed)
- received at least 3 courses of carboplatin or cisplatin therapy up to a maximum of 6 courses. Patients receiving more than 6 courses of therapy were included in this study, but data collection on those patients stopped after the sixth course.

Exclusion Criteria

Patients were excluded if they had thrombocytopenia, neutropenia, anaemia, severe GI disorders, peripheral neuropathy, ototoxicity, severe renal and hepatic failure, or electrolyte disturbance.

Data Collection

Data systems available at the time of the study could not provide the means for collecting the data necessary for this study; there were no computer-based systems that crossed all types of sites where patients can be treated. Therefore, the investigator created a unique, external data collection process that could be utilised to capture data in an everyday real world treatment setting for this study. Data were collected and compiled via a fax transmission process that scans directly, through optical mark and character recognition, into a computer database. This data collection method has been discussed in detail elsewhere.[15]

Costing Models

Direct medical cost models were developed to estimate total cost of resources utilised among patients treated with carboplatin or cisplatin. These models were designed to include specific resource variables that were measured in the study, along with specific standard costs assigned to each of the resource variables. The purpose of these models was to estimate the incremental difference in the cost of cisplatin versus carboplatin therapy in 2 cost analyses.

The resource variables in these models can be categorised into 2 types: treatment resource variables and toxicity-management resource variables. The resource variables, along with a short description of each, are listed by these classifications in tables I and II, respectively.

Because these were direct medical cost models, only direct medical costs related to the treatment and toxicity-management resource variables were considered. The following costs were not considered:

- personnel costs – defined as costs associated with hiring and maintaining administration, nursing, pharmacy and other personnel to perform scheduling, phone coverage, clerical duties, etc., but excluding any personnel costs associated with physician visits costs
- rent, equipment and overhead costs – defined as rent, equipment and overhead costs associated with chemotherapy administration
- supplies and disposal costs – defined as costs for the elimination of tubing, syringes, etc., associated with chemotherapy administration

Table IV. Patient sample and characteristics and treatment course description for each treatment group by cancer type

Variable	Nonsmall cell lung cancer			Small cell lung cancer			Ovarian cancer		
	carboplatin	cisplatin	test statistic	carboplatin	cisplatin	test statistic	carboplatin	cisplatin	test statistic
No. of patients	45	36		18	21		32	12	
No. of courses	193	152		77	101		150	61	
No. of courses per patient	4.3	4.2		4.3	4.8		4.7	5.1	
Mean age (SD)	62.3 (9.6)	63.5 (9.2)	p = 0.621[a]	67.2 (10.3)	59.5 (11.5)	p = 0.047[a]	64.1 (13.5)	55.3 (11.5)	p = 0.047[a]
Gender [no. of patients (%)]									
women	17 (37.8)	14 (38.9)	p = 1.000[b]	9 (50.0)	9 (42.9)	p = 0.752[b]	32 (100)	12 (100)	NA
men	28 (62.2)	22 (61.1)		9 (50.0)	12 (57.1)				
Disease stage[c] [no. of patients (%)]									
I	0 (0)	1 (2.9)	p = 0.972[d]	13 (76.5)	12 (63.2)	p = 0.481[b]	6 (19.4)	2 (16.7)	p = 0.858[d]
II	0 (0)	1 (2.9)		4 (23.5)	7 (36.8)		1 (3.2)	0 (0)	
III	18 (42.9)	12 (34.2)					16 (51.6)	7 (58.3)	
IV	24 (57.1)	21 (60.0)					8 (25.8)	3 (25.0)	
	Frequency missing[e] = 4			Frequency missing[e] = 3			Frequency missing[e] = 1		
Performance status [no. patients (%)]									
0	18 (41.9)	25 (71.4)	p = 0.492[d]	6 (35.3)	9 (47.4)	p = 0.508[d]	23 (76.7)	9 (75.0)	p = 1.000[d]
1	23 (53.5)	7 (20.0)		9 (52.9)	9 (47.4)		7 (23.3)	3 (25.0)	
2	2 (4.7)	3 (8.6)		2 (11.8)	0 (0)				
3				0 (0)	1 (5.3)				
	Frequency missing[e] = 3			Frequency missing[e] = 3			Frequency missing[e] = 2		

a P is probability from the Wilcoxon 2-Sample Test.

b P is probability from the Fisher's Exact Test (2-tail).

c Disease stage for small-cell lung cancer is divided into 2 categories where I equals limited disease and II equals extended disease.

d P is probability from the Wilcoxon 2-Sample Test.

e Frequency missing is the number of missing values.

NA = not applicable; **SD** = standard deviation.

Table V goes as a landscape table here.

- office staff and overheads – defined as the cost of the waiting room use, making an appointment, rent of the building and utilities.

It was estimated by oncology experts that these excluded costs mentioned in the previous paragraph would range from $US55.29 to $US70.29 per patient (1996 values) for the first hour and be higher thereafter, depending on the length of visit. Because fixed reimbursement rates are designed to incorporate some of the overhead costs, these rates (see next paragraph) were used instead of collecting true costs associated with chemotherapy administration. Additionally, indirect costs were not considered in our models.

Medication costs were estimated using specific medications' AWP which were determined from the 1996 Redbook.[16] The remaining costs were estimated using 2 sources to allow for sensitivity analysis: the 1996 Medicare Claims Database[14] and the 75th percentile of the 1996 PFR[13] based on 1996 Current Procedural Terminology (CPT) codes. These costs are presented in table III. In this paper, only PFR costs are reported. However, both cost calculations (PFR and Medicare) yielded similar results. When the low range (Medicare) to high range costs (PFR) were compared, while using AWP for all estimates, the overall differences in total mean costs associated with carboplatin versus cisplatin groups comparison were similar. Results using Medicare costs can be obtained from the authors upon request.

Types of Analysis

The cost of cisplatin and carboplatin was determined by cost per patient (CPP) and cost per course (CPC) analyses. CPP analyses answer questions from a physician/clinician's point of view. Although the drug cost of carboplatin is higher than that of cisplatin, previous research has suggested that the cost of toxicity management is higher for cisplatin because toxicities tend to accumulate for cisplatin over multiple courses of treatment.[9,17,18] A greater degree of renal dysfunction and other toxicities (with cisplatin) should result in a greater utilisation of healthcare resources over time i.e. the cost of managing these toxicities is not constant

Table V. Mean total costs per patient (CPP) and costs per course (CPC) for nonsmall cell lung cancer treatment resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	326.73	139.55	76.18	27.72	270.67	176.20	64.11	38.44
Hospitalisation days	213.89	678.68	49.87	318.84	403.47	774.55	95.56	202.25
Audiograms	1.64	7.71	0.38	3.76	3.08	10.37	0.73	5.16
CrCl measurements	9.80	19.82	2.28	10.36	5.44	25.60	1.29	7.87
Consultations	9.82	46.06	2.29	22.43	18.42	61.95	4.36	30.84
Other procedures	28.36	187.34	6.61	63.86	40.50	174.56	9.59	61.92
Radiation therapy	149.33	359.91	34.82	116.11	210.00	554.47	49.74	136.15
Chemotherapy agents	13 890.56	5025.63	3238.73	931.27	4858.16	1698.40	1150.62	577.25
Supportive agents	579.53	457.34	135.12	258.96	1095.63	964.87	259.49	179.63
Additional support agents								
magnesium	0.00	0.00	0.00	0.00	6.33	3.79	1.50	0.82
mannitol	0.00	0.00	0.00	0.00	20.15	8.87	4.77	1.60
potassium	0.18	0.83	0.04	0.41	14.11	7.44	3.34	1.49
diuretics	0.00	0.00	0.00	0.00	1.56	3.97	0.37	1.16
other	29.56	180.58	6.89	50.10	38.34	77.36	9.08	31.54
Growth factors	839.30	1792.37	195.69	455.59	113.54	387.88	26.89	192.92

AWP = average wholesale price; **CrCl** = creatinine clearance; **PFR** = physicians' fee reference; **SD** = standard deviation.

over each course, but gradually increases in subsequent courses. For example, if by course 3, 4 or 5, a cumulative toxicity effect for cisplatin was seen, the initial cost difference with carboplatin may be offset by the increased costs of treating these toxicities. Therefore, this type of CPP analysis shows a clearer picture of patient care throughout the entire treatment schema and helps identify healthcare inputs and costs associated with those inputs.

CPC analysis answers questions from a managed care/payer's point of view. A patient may have received anywhere from 3 to 6 courses; total patient costs tend to be higher as the number of courses increase. This type of analysis allows for an assessment of the entire treatment period and calculations of an overall average CPC of therapy, which may be of interest to managed care/payers. However, CPC analysis assumes a static healthcare input in the amount of toxicity management over each course of treatment.

Costing Model Formula

The algebraic model for both the mean CPC and mean CPP in US dollars was derived as follows:

$$\text{Mean CPC} = \frac{\sum_{P}\sum_{C}(\text{Units}_{P,C})(\text{CPU})}{C}$$

$$\text{Mean CPP} = \frac{\sum_{P}\sum_{C}(\text{Units}_{P,C})(\text{CPU})}{P}$$

where P is the total number of patients in each cancer type, C is the total number of courses for each patient, units are the total number of units for a particular resource variable used by patient P in course C, and CPU is the cost per unit of a particular resource variable.

Data and Sensitivity Analysis

Costing model implementation and analyses were performed using SAS[19] statistical software (Cary, North Carolina, USA). All data were kept strictly confidential and were reported in aggregate form only. Once the data were collected, verified

Table VI goes as a landscape table here.

Table VI. Mean total costs per patient (CPP) and costs per course (CPC) for nonsmall cell lung cancer toxicity-management resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	67.67	115.24	15.78	38.34	164.33	272.57	38.92	81.83
Hospitalisation days	264.44	708.52	61.66	289.67	175.00	568.99	41.45	283.93
Laboratory visits	509.11	674.01	118.70	143.98	211.06	317.73	49.99	70.97
Emergency room visits	31.11	93.56	7.25	39.27	4.86	40.65	1.15	20.01
Consultations	9.82	46.06	2.29	22.43	12.28	51.34	2.91	25.27
All toxicity-related procedures	49.10	121.55	11.45	30.49	182.51	442.64	43.23	112.42
Home healthcare								
days	15.47	81.46	3.61	39.54	84.58	395.41	20.03	85.82
antibacterials	19.56	131.20	4.56	63.35	11.20	67.23	2.65	32.72
other	0.00	0.00	0.00	0.00	12.14	50.06	2.88	7.43
Transfusions	89.16	258.86	20.79	92.46	22.67	76.24	5.37	37.96
Toxicity management agents	210.89	342.78	49.17	139.24	126.81	271.67	30.03	106.92

AWP = average wholesale price; **PFR** = physicians' fee reference; **SD** = standard deviation.

Table VII goes as a landscape table here.

and electronically databased, descriptive statistics such as mean and standard deviation were calculated for the outcome and cost analyses by cancer type (NSCLC, SCLC or ovarian cancer) and treatment group (cisplatin or carboplatin). For data on patient characteristics, normality of the continuous variables was assessed through exploratory data analysis using the Wilk's normality test. The Fisher's Exact Test (2-tail) was used to detect significant differences with the gender variable and a Wilcoxon 2-sample test was used to detect significant differences with the age variable. For the variables, disease stage and performance status, the Wilcoxon 2-sample test was used to test for significant differences. For the SCLC disease stage variable, the Fisher's Exact Test (2-tail) was used. The α probability level was set at 0.01.

With the exception of drug costs, all cost analyses were conducted using the PFR. As a sensitivity analysis, the PFR costs were substituted with the Medicare costs and results were compared. Both calculations yielded similar results, and therefore, only cost analyses using PFR are reported.

Results

Sample and Course Description

A total of 220 patients were enrolled in the study initially. Of these patients, 42 did not receive the required minimum number of 3 treatment courses. A total of 14 patients at only 1 site received both carboplatin and cisplatin during the treatment plan and they were excluded from the final analyses. Of these 14 patients, 9 switched from cisplatin to carboplatin and 5 switched from carboplatin to cisplatin. Therefore, a total of 56 patients did not meet the inclusion criteria and were dropped from the analyses. Thus, there were 164 evaluable patients (response rate of 74.2%). It is also important to point out that information on treatment received for the initial therapy (course 1) was not available for 11 of the 164 patients because treatment was received elsewhere. However, follow-up for these patients began at course 2 and at least a total of 3 additional courses of therapy were received. No

Table VII. Mean total costs per patient (CPP) and costs per course (CPC) for small cell lung cancer treatment resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	265.83	170.05	62.14	39.56	372.86	142.70	77.52	27.24
Hospitalisation days	573.61	1197.19	134.09	324.80	475.00	858.43	98.76	291.18
Audiograms	4.11	11.97	0.96	5.92	5.29	17.69	1.10	6.31
CrCl measurements	5.44	15.85	1.27	7.84	2.33	10.69	0.49	4.88
Consultations	40.33	93.64	9.43	41.54	31.57	105.66	6.56	37.71
Other procedures	144.50	358.80	33.78	123.34	22.86	66.12	4.75	31.00
Radiation therapy	23.33	98.99	5.45	47.86	500.00	612.76	103.96	182.17
Chemotherapy agents	7279.81	2685.45	1701.77	664.88	5506.74	3724.89	1144.97	190.71
Supportive agents	917.12	1238.90	214.39	213.88	1423.90	1389.20	296.06	165.73
Additional support agents								
magnesium	0.11	0.47	0.03	0.23	5.81	4.51	1.21	0.98
mannitol	0.00	0.00	0.00	0.00	23.31	9.98	4.85	1.79
potassium	1.33	3.88	0.31	1.08	13.14	9.41	2.73	1.87
diuretics	0.89	3.77	0.21	0.89	0.38	0.87	0.08	0.56
other	22.67	46.18	5.30	10.02	68.57	60.67	14.26	11.84
Growth factors	992.17	2596.47	231.93	591.18	1448.46	3265.87	301.16	527.12

AWP = average wholesale price; **CrCl** = creatinine clearance; **PFR** = physicians' fee reference; **SD** = standard deviation.

deaths occurred in either treatment groups (and in all 3 diseases) during the data collection period.

The final sample of patients consisted mostly of patients with NSCLC [81 (49.4%)], followed by ovarian cancer [44 (26.8%)] and SCLC [39 (23.8%)]. Table IV presents data on the patient sample and treatment course description. The total number of patients in each disease state along with the number of treatment courses is described.

Baseline Characteristics

No significant differences were found with any of the baseline characteristic variables (gender, disease stage, performance status and age) in any of the disease categories, indicating that both treatment groups for each type of cancer diagnosis were similar at the start of the study. The specific details of baseline characteristics for patients in each of the disease categories are described in table IV. For SCLC, the stage of disease was described as either limited or extended. For NSCLC and ovarian cancer, the stage of disease was described as stage I, II, III or IV. For more details on staging, please refer to Faber[20] and Gusberg and Runowicz.[21] Performance status was based on the Zubrod Scale (ECOG)[22] where: 0 = normal activity; 1 = symptoms, but nearly fully ambulatory; 2 = some bed time required, but needs to be in bed <50% of normal daytime; 3 = needs to be in bed >50% of normal daytime; and 4 = unable to get out of bed.

Mean CPP and Mean CPC

Table V describes the mean total costs of all treatment resource variables for patients with NSCLC, and table VI describes the mean total costs of all toxicity-management resource variables for this patient group. Table VII describes the mean total costs of all treatment resource variables for patients with SCLC, and table VIII describes the mean total costs of all toxicity-management resource variables for this group. Table IX describes the mean total costs of all treatment resource variables for patients with ovarian cancer, and table X describes the mean total costs of all

Table VIII goes as a land scape table here.

Table VIII. Mean total costs per patient (CPP) and costs per course (CPC) for small cell lung cancer toxicity-management resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	106.33	121.42	24.86	46.50	157.43	187.85	32.73	48.99
Hospitalisation days	320.83	703.21	75.00	359.57	225.00	470.04	46.78	225.32
Laboratory visits	145.00	215.41	33.90	66.10	298.29	727.50	62.02	138.29
Emergency room visits	9.72	41.25	2.27	19.94	25.00	62.75	5.20	29.86
Consultations	24.56	71.47	5.74	35.38	31.57	105.66	6.56	30.94
All toxicity-related procedures	152.50	479.47	35.65	80.64	112.88	369.98	23.47	122.36
Home healthcare								
days	198.17	642.65	46.32	166.74	132.57	516.62	27.56	113.39
IV antibacterials	0.00	0.00	0.00	0.00	9.19	42.12	1.91	19.21
IV fluids	0.00	0.00	0.00	0.00	1.14	5.24	0.24	0.27
other	55.04	134.16	12.87	41.98	9.90	45.39	2.06	2.95
Transfusions	22.67	96.17	5.30	26.49	97.14	163.16	20.20	54.86
Toxicity management agents	162.51	368.24	37.99	78.09	265.25	479.34	55.15	129.50

AWP = average wholesale price; **IV** = intravenous; **PFR** = physicians' fee reference; **SD** = standard deviation.

Table IX goes as a landscape table here.

toxicity-management resource variables in this group.

Overall Total Costs (Treatment Plus Toxicity Costs)

Table XI describes the overall mean total CPP and overall mean total CPC for treatment group by cancer type (both treatment and toxicity costs were considered).

NSCLC

The overall total CPP associated with the use of carboplatin was approximately $US9200 ($US17 345.03 vs $8106.84) higher than that for cisplatin in patients with NSCLC. The overall total CPC associated with the use of carboplatin was approximately $US2100 ($US4044.16 *vs* $US1920.05) higher than that for cisplatin in patients with NSCLC.

SCLC

The overall total CPP associated with the use of carboplatin was approximately $US200 ($US11 468.58 *vs* $US11 265.58) higher than that for cisplatin in patients with SCLC. The overall total CPC associated with the use of carboplatin was approximately $US340 ($US2680.96 *vs* $US2342.34) higher than that for cisplatin in patients with SCLC.

Ovarian Cancer

The overall total CPP associated with the use of carboplatin was approximately $US1200 ($US12 466.46 *vs* $US13 662.55) less than that for cisplatin in patients with ovarian cancer. The overall total CPC associated with the use of carboplatin was approximately $US30 ($US2659.49 *vs* $US2687.72) less than that for cisplatin in patients with ovarian cancer.

Discussion

When interpreting the results and drawing conclusions from this study, the following limitations need to be considered. First, the extent to which the results and conclusions can be generalised is limited only to the 3 diseases (SCLC, NSCLC and ovarian cancer) studied. Therefore, the data examined

Table IX. Mean total costs per patient (CPP) and costs per course (CPC) for ovarian cancer treatment resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	377.91	133.71	80.62	22.76	137.75	167.79	27.10	40.62
Hospitalisation days	65.63	197.54	14.00	51.77	1429.17	1270.37	281.15	400.69
Audiograms	0.00	0.00	0.00	0.00	3.08	10.68	0.61	4.74
CrCl measurements	6.13	20.64	1.31	7.92	4.08	14.15	0.80	6.27
Consultations	0.00	0.00	0.00	0.00	72.67	192.89	14.30	67.10
Other procedures	23.06	106.49	4.92	49.49	109.42	155.40	21.52	79.69
Radiation therapy	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Chemotherapy agents	10 433.74	3598.12	2225.86	883.67	6691.93	985.23	1316.45	584.32
Supportive agents	591.91	174.20	126.27	109.64	1107.14	849.26	217.80	311.33
Additional support agent								
magnesium	0.25	1.11	0.05	0.32	8.33	4.25	1.64	0.78
mannitol	0.00	0.00	0.00	0.00	22.46	12.29	4.42	2.20
potassium	0.75	2.58	0.16	0.79	15.00	9.82	2.95	1.77
diuretics	0.00	0.00	0.00	0.00	10.33	12.12	2.03	2.02
other	2.25	12.73	0.48	3.37	64.92	60.32	12.77	11.63
Growth factors	453.56	1039.38	96.76	282.94	1795.10	3208.42	353.13	705.57

AWP = average wholesale price; **CrCl** = creatinine clearance; **PFR** = physicians' fee reference; **SD** = standard deviation.

in this study may not be representative of patients with other disease states for which carboplatin and cisplatin are often used. It was believed, however, that the patient sample (although it was a convenience sample) from the treatment sites involved may have represented typical patients with SCLC, NSCLC and ovarian cancer. Because all treatment sites may differ to some degree with respect to resources utilised, patient population served and care patterns delivered, the results of this study cannot be generalised to settings that differ substantially from the study sites.

Second, some may argue that the results are limited because this study was not of a randomised, controlled design and, therefore, the results are less credible. However, it is important to point out that the study design was chosen so that the effectiveness in a real world, everyday treatment setting could be measured where no study protocols are used as compared with clinical trials which measure efficacy under controlled conditions. An advantage of effectiveness evaluation is that it provides clinicians with a clear picture of what is occurring and which resources are consumed in a particular setting. Conversely, it is difficult to control for different practice patterns of prescribing physicians and/or sites.

Although the patients and the treatment sites were not selected randomly, baseline characteristics indicate that both treatment groups were similar. These similarities may be a result of the following considerations that were taken into account when selecting the sample: different geographical areas of the US; sites representing a mix of designated cancer centres, managed-care sites, outpatient clinics and medical centres/private hospitals; sites with sufficient numbers of patients with lung and ovarian cancer along with sites that used either carboplatin, cisplatin or both.

Third, sample sizes were small and therefore the power to find significant differences was low. Fourth, the investigator relied on the individual sites for data collection and, therefore, the data only indicate the patient information that was obtainable. Based on individual site visits, the data collected in this study were reliable as shown by

Table X goes as a landscape table here.

Table X. Mean total costs per patient (CPP) and costs per course (CPC) for ovarian cancer toxicity-management resource variables

Resource variable	Mean PFR and AWP costs ($US; 1996 values)							
	carboplatin				cisplatin			
	CPP		CPC		CPP		CPC	
	mean	SD	mean	SD	mean	SD	mean	SD
Clinic visits	87.00	136.22	18.56	37.15	65.25	105.74	12.84	31.11
Hospitalisation days	43.75	160.27	9.33	75.28	262.50	648.38	51.64	217.51
Laboratory visits	177.63	292.77	37.89	71.43	580.00	459.36	114.10	148.99
Emergency room visits	5.47	30.94	1.17	14.29	14.58	50.52	2.87	22.41
Consultations	6.91	39.07	1.47	18.04	18.42	63.80	3.62	28.30
All toxicity-related procedures	15.41	44.00	3.29	13.45	92.28	227.27	18.15	37.88
Home healthcare								
days	97.88	400.67	20.88	79.16	297.25	901.43	58.48	309.93
other	16.31	67.89	3.48	3.74	61.68	138.64	12.13	48.24
Transfusions	21.25	78.08	4.53	24.49	0.00	0.00	0.00	0.00
Toxicity management agents	39.66	59.28	8.46	20.53	799.21	539.21	157.22	321.74

AWP = average wholesale price; **PFR** = physicians' fee reference; **SD** = standard deviation.

Table XI. Overall mean total costs per patient (CPP) and costs per course (CPC) for each treatment group by cancer type

Resource variable	Mean total PFR and AWP costs ($US; 1996 values)			
	carboplatin		cisplatin	
	CPP	CPC	CPP	CPC
Nonsmall cell lung cancer				
Treatment resource variables	16 078.70	3748.90	7099.40	1681.44
Toxicity-management resource variables	1266.33	295.26	1007.44	238.61
Total	**17 345.03**	**4044.16**	**8106.84**	**1920.05**
Small cell lung cancer				
Treatment resource variables	10 271.25	2401.06	9900.22	2058.46
Toxicity-management resource variables	1197.33	279.90	1365.36	283.88
Total	**11 468.58**	**2680.96**	**11 265.58**	**2342.34**
Ovarian cancer				
Treatment resource variables	11 955.19	2550.43	11 471.38	2256.67
Toxicity-management resource variables	511.27	109.06	2191.17	431.05
Total	**12 466.46**	**2659.49**	**13 662.55**	**2687.72**

AWP = average wholesale price; **PFR** = physicians' fee reference.

the overall reliability measure of 0.999.[15] Some patient information, however, may not have been captured due to logistical problems. For example, all adverse event data may not have been collected. However, these deficiencies would not have altered resources utilised.

Finally, the costs used in this study were not true costs of the resource variables utilised. Due to the difficulty of obtaining true costs, predetermined, discounted fixed payment rates from 2 sources (Medicare and PFR) were used. These dollar values may not represent true costs or true charges. It was believed that these 2 national sources were, however, conservative measures.

Rees[23] reported that cost assessment in oncology should involve costs of treatment and procedures, total hospital costs, transportation costs, and expenditures incurred by the patient and family. In this study, only direct medical costs were assessed. Thus, the total cost estimates reported do not reflect all costs associated with the treatment.

Previous studies produced mixed conclusions about the use of carboplatin and cisplatin in ovarian cancer. Alberts[9] and Calvert and Urie[10] stated that the overall costs were lower for carboplatin while George et al.[11] stated that the overall costs were similar. Although these studies serve as a foundation for economic analyses, they were conducted using protocol-driven clinical trials. Due to the differences in the results of the 3 studies, absence of study protocols in everyday treatment settings, and lack of prospective, economic analyses in the literature in lung and ovarian cancer, it was clear that more prospective economic research was needed with carboplatin and cisplatin therapy in the treatment of lung and ovarian cancer.

This study adds to the literature by providing results from a prospective real world assessment of current treatments. However, further research is needed in this area. Future studies could be conducted to include more patients, more sites, true cost data, indirect costs, miscellaneous costs, better patient follow-up information and patient's quality of life.

Conclusion

The total costs (treatment plus toxicity costs) associated with the use of carboplatin were higher than those of cisplatin in patients with NSCLC, similar in SCLC but lower in ovarian cancer. These results indicate that treatment and toxicity costs vary depending on cancer type, despite the use of the same 2 drugs. Because of study limitations, it is not appropriate to generalise the findings to other diseases, even if the same drugs are being com-

pared and the diseases are similar (NSCLC *vs* SCLC).

From a payer's perspective, it is crucial to evaluate total costs (treatment and toxicity costs) of a disease over the entire treatment period when considering the use of various drugs for therapy in disease management. Although the acquisition drug cost may be higher for a specific agent, the overall costs may be less over time. Therefore, by understanding all of the costs involved in disease management, one can provide the most cost-effective therapy overall. In this instance, the use of carboplatin has more cost savings than cisplatin in ovarian cancer, similar savings in SCLC, and less cost savings in NSCLC in a general practice oncology setting.

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