Pergamon

European Journal of Cancer, Vol. 34, No. 12, pp. 1894–1901, 1998

Printed in Great Britain
0959-8049/98/$—see front matter

PII: S0959-8049(98)00260-3

Original Paper

Cost-effectiveness Analysis of Paclitaxel and Cisplatin Versus Cyclophosphamide and Cisplatin as First-line Therapy in Advanced Ovarian Cancer. A European Perspective

K. Berger,[1] T. Fischer[1] and T.D. Szucs[2]

[1]Medical Economics Research Group, Prinzregentenst. 72, D-81675 Munich, Germany; and [2]Centre for Pharmacoeconomics, School of Pharmacy, University of Milan, Milan, Italy

Paclitaxel is a new cytotoxic agent that has demonstrated significant activity in advanced ovarian cancer. The aim of this study was to determine the cost structure of advanced ovarian cancer and the cost-effectiveness of paclitaxel–cisplatin (PC) combination therapy compared with a standard cyclophosphamide–cisplatin (CC) regimen as first-line therapy. The analysis was performed separately for six European countries: Germany, Spain, France, Italy, The Netherlands and the U.K. The study was conducted from the national health service payer's perspective. The total cost of treatment per patient (six cycles of chemotherapy) in the six European countries varied between a minimum of US$4,926 in the U.K. and US$12 578 in Germany for the CC regimen and between US$13 038 and US$24 487 for the PC regimen (April 1996). Since the new regimen improved life expectancy by 1.283 years compared with CC, the incremental cost-effectiveness of PC was calculated to be between US$6,403 per 5-year saved in the U.K. and US$11 420 per life-year saved in Italy. Overall, the cost-effectiveness of PC compares favourably with other oncological interventions. The findings of this study suggest that healthcare decision makers should consider paclitaxel, in combination with cisplatin, as a cost-effective first-line therapy for patients with advanced ovarian cancer. © **1998 Elsevier Science Ltd. All rights reserved.**

Key words: cost-effectiveness analysis, paclitaxel, cyclophosphamide, cisplatin, advanced ovarian cancer, European perspective
Eur J Cancer, Vol. 34, No. 12, pp. 1894–1901, 1998

INTRODUCTION

WHO DATA show an incidence of 645 000 cases of cancer in the European Community in 1990. Included in this are approximately 28 000 cases of ovarian cancer [1]. Ovarian cancer is the sixth most common form of cancer worldwide and has the highest mortality rate of all gynaecological cancers [2]. Early stages of ovarian cancer are usually asymptomatic, and most symptoms of the disease are manifestations of advanced disease [3]. Thus, the majority of patients with ovarian cancer present with advanced disease (stage III–IV according to International Federation of Gynaecology and Obstetrics (FIGO) classification). In these patients, typically after careful cytoreductive surgery, systemic platinum-based combination chemotherapy forms the cornerstone of successful management. Whilst initial response rates are high, however, the long-term prognosis of patients with advanced ovarian cancer remains poor: only 10–25% of women survive 5 years after diagnosis [5].

Paclitaxel (Taxol®), which is produced semisynthetically from needles and twigs of *taxus* plants, is a new cytotoxic agent with a novel mechanism of action that has demonstrated significant activity in advanced ovarian cancer. Initial trials in patients with advanced disease, who were either heavily pretreated with platinum or had refractory disease, showed a dramatic and prolonged response to paclitaxel monotherapy [6]. In a randomised clinical study, the Gynaecologic Oncology Group compared paclitaxel and cisplatin (PC) as first-line chemotherapy with the standard therapy of cyclophosphamide and cisplatin (CC) (GOG 111) [7]. The results showed a significant improvement in overall response rate, complete response, progression-free survival and overall

Correspondence to K. Berger.
Received 15 Oct. 1997; revised 18 May 1998; accepted 12 Jun. 1998.

survival for the paclitaxel group [7]. These findings have led to the suggestion that the PC combination should be given in preference over CC as first-line chemotherapy for patients with advanced ovarian cancer [8].

As the focus on cost containment among decision makers becomes more intense, the medical benefits could easily be diminished by the fact that therapy with paclitaxel might appear to be more expensive than other chemotherapies. Therefore, economic evaluations are necessary. Economic evaluations compare the costs and consequences of alternative treatments for advanced ovarian cancer with respect to medical improvements. The cost implications of treating advanced ovarian cancer with PC have already been examined from a Canadian perspective: the first study concerning second- and third-line chemotherapy with different regimens including PC showed total average costs of Can$53 000 (US$37 900) per patient [9]. Another cost analysis showed that the incremental cost-effectiveness of PC over conventional first-line therapy was Can$20 355 (US$14 500) per life-year saved [10]. In a different economic analysis of the GOG 111 study conducted from the perspective of the US healthcare provider, combination therapy with PC cost an additional US$19 820 per life-year saved compared with CC when patients were treated in the hospital, and US$21 222 per life-year saved when patients were treated in an outpatient setting [11]. Finally, in an Italian study, the cost structure of PC versus CC as first-line therapy was analysed. They calculated the incremental cost-effectiveness for paclitaxel with US$19 603 per life-year saved [12].

However, the cost of care structure of usual care of advanced ovarian cancer in Europe, and the economic outcomes of treatment with PC chemotherapy, have not been examined previously. Thus, the aim of this retrospective study, conducted from the national health service payer's perspective of six European countries, was to determine the cost structure of advanced ovarian cancer and the cost-effectiveness of PC combination therapy as first-line chemotherapy for advanced ovarian cancer compared with a standard CC regimen, using the results of the GOG 111 study [11].

PATIENTS AND METHODS

The GOG 111 study

In this study, a retrospective analysis was performed on 386 women treated with cisplatin (75 mg/m^2 at a rate of 1 mg/min) plus either cyclophosphamide (750 mg/m^2) or paclitaxel (135 mg/m^2 over 24 h) for advanced ovarian cancer in the GOG 111 study (Table 1). To be included in the GOG 111 study, patients had to have histologically confirmed stage III epithelial ovarian cancer with residual masses > 1 cm after surgery or stage IV disease. No patient had received prior chemotherapy or radiation therapy for ovarian cancer and all patients had a GOG performance status score of 0, 1 or 2. Other inclusion criteria included normal baseline blood counts and normal renal and hepatic function. Patients with a history of cardiac arrhythmias and those receiving antiarrhythmic drugs were not eligible for inclusion. All chemotherapeutic agents were administered intravenously and patients received a total of six cycles of chemotherapy, with each cycle administered at 3 weekly intervals. Because administration of paclitaxel can cause hypersensitivity reactions, patients assigned to the PC group were premedicated according to local treatment patterns.

Table 1. *Patient clinical characteristics at baseline* [7]

Parameter	Treatment	
	PC (n = 184)	CC (n = 202)
Mean age, years (range)	59 (20–84)	60 (27–80)
Stage (no. of patients)		
III	123	129
IV	61	73
GOC performance status (no. of patients)		
0	56	55
1	97	109
2	31	38
No. of patients with ascites > 100 ml	163	173

CC, cyclophosphamide–cisplatin; GOC, Gynaecologic Oncology Group; PC, paclitaxel–cisplatin.

Among 216 patients with measurable disease, 73% of PC recipients responded to therapy compared with 60% of patients in the CC group (P = 0.01), and the median progression-free survival was significantly longer (P < 0.001) among PC recipients (18 months versus 13 months among CC treated patients). The median overall survival was also significantly longer (P < 0.001) in the PC group (38 months versus 24 months among CC treated patients) [7]. For the purposes of the present economic analysis, the outcome of interest was median overall survival.

Study objectives

The objectives of this economic analysis, conducted from the national health service payer's perspective, were to determine the cost structure of treating advanced ovarian cancer and to determine the cost-effectiveness of PC as first-line chemotherapy for women with advanced ovarian cancer compared with the standard platinum-based combination regimen.

Elaboration of costs

In general, costs are defined as the result of resource consumption multiplied by the price for the resource. Therefore, the quantitative resource consumption as well as the prices were collected separately. The resource consumption was determined quantitatively on the basis of structured face-to-face interviews with experts (Table 2) treating advanced ovarian cancer, delivering the information required to evaluate the direct costs induced by chemotherapy of advanced ovarian cancer and the GOG 111. The interviews yielded country-specific data about duration and extent of drug treatment (e.g. co-medication) as well as frequency of consultations and laboratory tests. GOG 111 was the data source

Table 2. *Sample of medical specialists*

	Gynaecologists	Oncologists	Internal medicine	Total
Germany	6	0	1	7
Spain	0	8	0	8
France	0	6	0	6
Italy	4	3	0	7
The Netherlands	0	4	0	4
U.K.	2	2	0	4
Total	12	23	1	36

for information on chemotherapy dosage, number of treatment cycles and their toxicity profile (adverse events). Additional interviews and literature searches, depending on the specific country, yielded prices for drugs and other resources, e.g. hospital stay, consultations, visits to validate the interview results. To achieve comparable results, all costs were calculated in US$.

The prices for chemotherapy were obtained from telephone interviews with hospital pharmacists and official drug price lists (Table 3). The calculation was performed for a body surface area of 1.76 m^2 at doses of 135, 75 and 750 mg/m^2 for paclitaxel, cisplatin and cyclophosphamide, respectively. The cost of co-medication administered with each cycle of chemotherapy (e.g. antibiotics, rehydration, antiemetics), including premedication for PC recipients, was also determined through the same sources. The costs of hospital or day clinic stay were obtained from interviews and hospital price lists (Table 3). The average costs of laboratory tests/investigations were determined in the same way (Table 3).

Briefly, the interviews were performed to determine the following cost categories:

1. medication: chemotherapy (paclitaxel, cisplatin and cyclophosphamide), treatment of adverse events, including allergic reactions, neurological symptoms, nephrotoxicity, alopecia, fever, gastrointestinal symptoms, anaemia, thrombocytopenia, leucopenia and neutropenia (drugs, dosage and duration of treatment);
2. hospitalisation (during administration of chemotherapy): average duration of hospital stay per cycle;
3. consultations/laboratory tests/investigations: average number of consultations/laboratory tests/investigations per patient for an overall course of treatment (six cycles).

Determination of effectiveness and cost-effectiveness analysis

The effectiveness endpoint in this study was life-years saved under PC therapy. The first step in the analysis was to calculate the specific life expectancy of PC and CC treated patients using the DEALE (declining exponential approximation of life expectancy) approach [13]. This algorithm, which is simple to use and has been shown to closely estimate life expectancy based on actuarial methods, calculates the specific life expectancy of a patient from the disease-specific mortality rate and the mortality rate of the standard population of a given age and gender. The GOG 111 study provided the median age of both treatment groups and disease-specific mortality. Further tables of vital statistics provided the country-specific life expectancy. Thus, the specific life expectancy could be determined in years for each treatment group (Table 4). In the final step of the analysis, the incremental life-years saved in the PC group was determined by subtracting the specific life expectancy in the CC group from the specific life expectancy in the PC group. The incremental cost-effectiveness of PC was subsequently calculated as follows:

$$\text{Cost per life-year saved} = \frac{\Delta\text{Total cost-complete course of treatment (PC} - \text{CC)}}{\Delta\text{Specific life expectancy (PC} - \text{CC)}}$$

Sensitivity analyses

The robustness of the results of this economic analysis were tested using a series of sensitivity analyses. These tests take into consideration, due to uncertainties, lack of precise cost of illness data and, therefore, use data from expert interviews and literature research. First, the increase in specific life expectancy associated with PC therapy was varied by ± 50%. Second, the costs of medication (chemotherapy and co-medication) and hospitalisation were varied by ± 20%, as described for a previous economic analysis of the GOG 111 data and the prices in most of the included countries varied according to this range [10].

RESULTS

Cost structure

In patients receiving standard CC, the overall net expenditure over all cycles varied between a minimum of approximately US$4,926 in the U.K. and a maximum of US$12 578 in Germany. (Approximately US$9,290 are obtained in Spain, US$8,502 in France, US$6,578 in Italy and US$6,537 in The Netherlands). The use of PC yielded minimum total costs of approximately US$13 038 in the U.K. and maximal total costs of US$24 487 in Germany (approximately

Table 3. Source of costs for medication, hospital stay and consultation and laboratory tests

	Medication	Hospital/day clinic stay	Consultations/laboratory tests
Germany	Pharmaceutical Index (Rote Liste) 1996	Federal Statistical Office (Statistisches Jahrbuch 1995)	Standard criterion of assessment (Einheitlicher Bewertungsmaßstab) 1996
Spain	Telephone interviews with four pharmacists and three hospital administrators	Telephone interviews with seven hospital administrators, doctors	Five telephone interviews with hospital administrators, doctors
France	Telephone interviews with five hospital pharmacists (averages were used), Vidal 1995	Telephone interviews with five hospitals in Rennes and Paris	Five telephone interviews with heads of laboratories in Rennes and Paris
Italy	Pharmaceutical Information list (Informatore Farmaceutico)	Telephone interviews with seven hospital administrators	Eight telephone interviews with public and private laboratories/average
The Netherlands	Official price list, publication in Drug Manual	Telephone interviews with account departments of five hospitals	Telephone interviews with account departments of five hospitals (of which two were private)
U.K.	British National Formulary	Normal published prices by British Medical Association	Published prices by British Medical Association

Table 4. Life expectancy for Germany, Spain, France, Italy, The Netherlands and the U.K.

	Germany			Spain			France			Italy			The Netherlands			U.K.		
Treatment	CC	PC	Difference*	CC	PC	Difference*	CC	PC	Difference*	CC	PC	Difference*	CC	PC	Difference*	CC	PC	Difference*
Life expectancy (years)	22.4	22.4	0	23.4	23.4	0	24.4	24.4	0	23.1	23.1	0	23.2	23.2	0	22.1	22.1	0
Median overall survival (years)	2	3.2	1.2	2	3.2	1.2	2	3.2	1.2	2	3.2	1.2	2	3.2	1.2	2	3.2	1.2
Disease-specific mortality rate	0.217	0.347	0.130	0.217	0.347	0.130	0.217	0.347	0.130	0.217	0.347	0.130	0.217	0.347	0.130	0.217	0.347	0.130
Life expectancy (years)	2.557	3.829	1.272	2.570	3.857	1.287	2.581	3.883	1.302	2.565	3.848	1.283	2.567	3.851	1.284	2.553	3.820	1.267

*PC – CC. PC, paclitaxel–cisplatin; CC, cyclophosphamide–cisplatin.

Table 5. Incremental costs for paclitaxel–cisplatin (PC) versus cyclophosphamide–cisplatin (CC) in US$

Cost category	Germany	Spain	France	Italy	The Netherlands	U.K.
Total costs for CC	12 578	9,290	8,502	6,578	6,537	4,926
Total costs for PC	24 487	17 520	17 150	21 230	16 547	13 038
Incremental costs	11 909	8,230	8,648	14 652	10 010	8,112

Table 6. Cost per life-year saved for paclitaxel–cisplatin (PC) versus cyclophosphamide–cisplatin (CC) in US$

Cost category	Germany	Spain	France	Italy	The Netherlands	U.K.
Incremental costs	11 909	8,230	8,648	14 652	10 010	8,112
Incremental life expectancy of PC group versus CC group	1.272	1.287	1.302	1.283	1.284	1.267
Cost per life-year saved	9,362	6,395	6,642	11 420	7,796	6,403

US$21 230 in Italy, US$17 520 in Spain, US$17 150 in France and US$16 547 in The Netherlands).

Compared with the CC regimen, drug costs, hospitalisation costs, costs of consultations/laboratory tests/investigations and the costs of treating adverse events were higher among PC recipients. Overall, the incremental cost of a complete course of PC chemotherapy was US$11 909 in Germany, US$8,230 in Spain, US$8,648 in France, US$14 652 in Italy, US$10 010 in The Netherlands and US$8,112 in the U.K. (Table 5).

Drug costs (chemotherapy plus co-medication) accounted for the largest proportion of treatment costs among PC recipients (average 59.2%; maximum 77.4% in the U.K.), whilst hospitalisation costs accounted for an average of 53.9% with a maximum of 75.7% (France) for overall treatment costs among patients treated with CC.

Effectiveness and cost-effectiveness

The median age of PC and CC treated patients in the GOG 111 study was 59 and 60 years, respectively [7]. The age, gender and race adjusted life expectancy of these patients was 22.1–24.4 years [14], whilst the median survival among PC and CC treated patients in the GOG 111 study was 3.2 and 2 years, respectively. Using the DEALE approach, the calculated specific average life expectancy in the PC and CC treatment groups was 3.848 and 2.565 years, respectively, giving an average incremental life expectancy among PC recipients of 1.283 years (Table 4). The incremental cost-effectiveness (cost per life-year saved) of PC compared with CC was, therefore, calculated at US$9,362 in Germany, US$6,395 in Spain, US$6,642 in France, US$11 420 in Italy, US$7,796 in The Netherlands and US$6,403 in the U.K. (Table 6). The cost-effectiveness ratios of other oncological therapies for comparison are shown in Table 7.

Sensitivity analyses

As the greatest difference between the two regimens related to the costs of chemotherapy/co-medication and hospitalisation, these parameters were further investigated in sensitivity analyses (Table 8). Presenting, for example, the cost sensitivity analysis of Italy with an assumption of an incremental increase in specific life expectancy of 1.283 years and that the costs of drugs and hospitalisation for the PC regimen are each reduced by an arbitrary figure of 20%, then the cost per life-year saved among PC recipients decreases to US$9,551 and US$10 477, respectively (Table 8). Increasing the costs of PC chemotherapy and hospitalisation by up to 20% revealed a predictable increase in the respective cost-effectiveness ratios. The sensitivity analyses of Germany, Spain, France, The Netherlands and the U.K. brought similar results (Table 8). Nevertheless, the incremental cost-effectiveness of PC under these conditions remained comparable with other oncological therapies.

The incremental increase in specific life expectancy associated with PC was also subjected to sensitivity analyses. Under base-case conditions, increasing the incremental increase in specific life expectancy by 50% to 1.925 years in Italy decreased the cost-effectiveness of PC to US$7,611 per life-year saved. Whilst decreasing the specific life expectancy by 50% to 0.642 years increased the cost-effectiveness of PC to US$22 822 per life-year saved in Italy, the cost-effectiveness ratio of PC versus CC under such conditions remained within acceptable limits. There was only a small difference between the other five countries concerning the calculation with 1.925 and 0.642 years of life expectancy. For the assumed higher and lower life expectancies, sensitivity analyses were also carried out for decreased and increased drug and hospitalisation costs.

DISCUSSION

On the basis of the findings of the GOG 111 study, we decided to perform an incremental cost-effectiveness analysis (i.e. cost per life-year saved). In contrast to cost-benefit and cost-minimisation analyses, which express costs and consequences in monetary units, a cost-effectiveness analysis expresses costs in monetary units and effectiveness (outcomes) in non-monetary units. If two or more interventions have the same treatment objective but different degrees of effectiveness, then a cost-effectiveness analysis is the preferred method. One of the advantages of incremental cost-effectiveness analysis is that it provides healthcare decision-makers with a common denominator by which various healthcare interventions can be tentatively compared, which may aid decision making with regard to optimal allocation of scarce resources. In a recent analysis of 500 life-saving interventions in the U.S.A., for example, Tengs and colleagues reported that the cost of postsurgical chemotherapy for premenopausal women with breast cancer was US$18 000 per life-year saved [14]. Among non-oncological interventions, the incremental cost-effectiveness of β-adrenoreceptor antagonists

Table 7. Cost-effectiveness ratios of different oncological therapies

Intervention	Costs/life-year (US$)	Reference
Routine CEA monitoring colon carcinoma	31 000–6 600 000	[15]
ABMT for relapse metastatic Hodgkin's disease	421 000	[16]
Bone marrow transplant and high (versus standard) chemotherapy for breast cancer	129 179	[17]
ABMT metastasing breast cancer CA	115 800	[17]
Chemotherapy ANLL	80 300	[18]
Adjuvant CMF, 75 years	44 000	[19]
Postsurgical chemotherapy for woman with breast cancer age 60 years	22 105	[20]
Postsurgical chemotherapy for premenopausal woman with breast cancer	18 107	[20]
Interferon alpha-2b in hairy cell leukaemia	13 800	[21]
Paclitaxel as first-line chemotherapy (six European countries)	6400–11 400	
Adjuvant CMF, 45 years	4900	[20]
Tamoxifen in advanced breast cancer	810	[22]

CEA, carcinoembryonic antigen; ABMT, autologous bone marrow transplantation; CMF, cyclophosphamide, methotrexate fluorouracil; ANLL, acute nonlymphocytic leukaemia.

Table 8. *Sensitivity analysis for Germany, Spain, France, Italy, The Netherlands and the U.K. All costs are in US$ (April* 1996*)*

	Increase in survival (years)																	
	Germany			Spain			France			Italy			The Netherlands			U.K.		
Assumption change	0.636	1.272	1.908	0.644	1.287	1.931	0.651	1.302	1.953	0.642	1.283	1.925	0.642	1.284	1.926	0.634	1.267	1.90
None (base-case, US$)	18 724	9,362	6,241	12 790	6,395	4,263	13 284	6,642	4,428	22 822	11 420	7,611	15 594	7,796	5,198	12 806	6,403	4,269
Drug costs US$*																		
Decrease cost of PC regimen by																		
10%	16 726	8,363	5,575	11 248	5,624	3,749	11 900	5,950	3,967	20 955	10 485	6,988	14 028	7,014	4,676	11 212	5,606	3,737
15%	15 726	7,863	5,242	10 478	5,239	3,493	11 208	5,604	3,736	20 021	10 018	6,677	13 250	6,625	4,417	10 416	5,208	3,472
20%	14 726	7,363	4,909	9,708	4,854	3,236	10 516	5,258	3,505	19 087	9,551	6,366	12 472	6,236	4,157	9,620	4,810	3,207
Increase cost of PC regimen by																		
10%	20 728	10 364	6,909	14 324	7,162	4,775	14 668	7,334	4,889	24 690	12 355	8,234	17 142	8,571	5,714	14 398	7,199	4,799
15%	21 728	10 864	7,243	15 092	7,546	5,031	15 360	7,680	5,120	25 624	12 822	8,546	17 920	8,960	5,973	15 196	7,598	5,065
20%	22 728	11 364	7,576	15 862	7,931	5,287	16 052	8,026	5,351	26 558	13 289	8,857	18 700	9,350	6,233	15 992	7,996	5,331
Hospitalisation costs US$																		
Decrease cost of hospitalisation for PC regimen by																		
10%	17 848	8,924	5,949	12 428	6,214	4,143	12 492	6,246	4,164	21 880	10 948	7,297	14 064	7,032	4,688	12 602	6,301	4,201
15%	17 408	8,704	5,803	12 250	6,125	4,083	12 096	6,048	4,032	21 408	10 712	7,140	13 734	6,867	4,578	12 502	6,251	4,167
20%	16 970	8,485	5,657	12 070	6,035	4,023	11 700	5,850	3,900	20 937	10 477	6,983	13 404	6,702	4,468	12 400	6,200	4,134
Increase cost of hospitalisation for PC regimen by																		
10%	19 606	9,803	6,535	13 144	6,572	4,381	14 076	7,038	4,692	23 765	11 892	7,926	15 384	7,692	5,128	13 008	6,504	4,336
15%	20 046	10 023	6,682	13 322	6,661	4,441	14 472	7,236	4,824	24 237	12 128	8,083	15 714	7,857	5,238	13 110	6,555	4,370
20%	20 486	10 243	6,829	13 502	6,751	4,501	14 868	7,434	4,956	24 708	12 364	8,240	16 044	8,022	5,348	13 212	6,606	4,404

*Cost of chemotherapy and co-medication. PC, paclitaxel–cisplatin.

for low-risk patients following myocardial infarction was estimated at US$16 897 per life-year saved [14]. Whilst the latter study was performed in the U.S.A. and, therefore, its findings are not directly comparable with other countries, these figures indicate the acceptable cost to society of many life-saving medical interventions. The incremental cost-effectiveness of US$6,403 to US$11 420 per life-year saved for patients treated with PC for advanced ovarian cancer in six European countries, therefore, compares favourably with other life-saving interventions. Furthermore, even if the improvement in survival is reduced by 50% to 0.642 years, the incremental cost-effectiveness of PC continues to remain acceptable when compared with other oncological therapies. The analysis shows some differences between the European countries concerning the proportion between chemotherapy drug costs and hospitalisation costs. In France, the hospitalisation costs are very high (75.7% of all costs) in the CC treatment group, whereas in the U.K. the hospitalisation costs are nearly as high as the other costs (32.6% for hospitalisation versus 21.1% for treatment and 37.1% for laboratory and consultation costs).

Whilst the present study is limited by the fact that it was a retrospective analysis and that the cost structure was principally determined by expert opinion from interviews with a limited number of physicians, it does provide an interesting insight into the cost structure of treating advanced ovarian cancer. We found that the main cost drivers in the treatment of advanced ovarian cancer in the six European countries are drug and hospitalisation costs, which confirms the findings of previous economic analyses of the GOG 111 study from Canadian and US healthcare perspectives [9–11]. When the contribution of the different costs included in the present analysis are compared between the two regimens, it can be seen that drug-related costs accounted for the greatest difference between the PC and CC regimens.

The magnitude of the difference in hospitalisation costs between the two chemotherapy regimens may be explained by the fact that paclitaxel was given as a continuous 24 h intravenous infusion, which requires more intensive (and, therefore, more costly) nursing time. Reducing the duration of infusion of paclitaxel may be one way in which the costs of hospitalisation could be reduced. Indeed, Eisenhauer and associates reported similar clinical efficacy by 3 h and 24 h infusions of paclitaxel [23]. The superiority of a 3 h infusion of paclitaxel (175 mg/m^2) in combination with cisplatin over a standard CC regimen was recently confirmed in a large multicentre trial whose results were presented at the 1997 annual meeting of the American Society of Clinical Oncology. The PC combination led to less febrile neutropenia than the CC therapy [22].

Since the goal of modern medicine is to improve patients' quality, as well as the quantity, of life, a potential limitation of the GOG 111 study (on which the present economic analysis was based) is that patients' quality of life during the extended survival period associated with PC chemotherapy was not assessed. Indeed, an improvement in life expectancy does not necessarily confer an improvement in quality of life among cancer patients, since long-term adverse events of cytotoxic drug therapy (e.g. peripheral neuropathy) can diminish a patients' quality of life; furthermore, the management of such adverse effects may incur additional resource costs. In addition to improving overall life expectancy, the PC regimen was associated with a significantly increased duration of progression-free survival compared with standard CC chemotherapy in the GOG 111 study [7]. Thus, the ability of PC to delay disease progression, which is the most important factor in determining the quality of life of patients with advanced cancer, is likely to have improved the quality of life of surviving patients. Therefore, the cost utility of PC (i.e. cost per quality-adjusted life-year saved) as first-line therapy in advanced ovarian cancer warrants further investigation. Indeed, a cost utility analysis would enable the effects of this innovative chemotherapy regimen on patients' quality of life and survival to be considered together, by converting both in a common unit of measure. Moreover, recent clinical trials have shown that carboplatin, a platinum compound with a better therapeutic index than the one of cisplatin, is safe and effective when used in combination with paclitaxel in patients with advanced ovarian cancer and the cost-effectiveness of this combination regimen warrants further investigation.

In conclusion, paclitaxel, in combination with cisplatin, is clinically more effective than a standard CC regimen (in terms of duration of progression-free and overall survival) as first-line chemotherapy following incomplete surgical resection of advanced ovarian cancer. From the national health service payer's perspective of six selected European countries (Germany, Spain, France, Italy, The Netherlands and the U.K.), the incremental cost-effectiveness of PC was calculated at US$6,403 to US$11 420 per life-year saved, which compares favourably with other oncological and non-oncological interventions. These findings suggest that healthcare decision makers should consider PC as a cost-effective therapeutic option for first-line management of advanced ovarian cancer.

1. International Agency for Research on Cancer. Facts and figures of cancer in the European community. Lyon, 1993.
2. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of eighteen major cancers in 1985. *Int J Cancer* 1993, **54**(4), 594–606.
3. Lorigan PC, Crosby T, Coleman RE. Current drug treatment guidelines for epithelial ovarian cancer. *Drugs* 1996, **51**(4), 571–584.
4. The new FIGO stage grouping for primary carcinoma of the ovary (1985). *Gynecol Oncol* 1986, **25**, 383.
5. Allen DG, Baak J, Belpomme D, *et al.* Advanced epithelial ovarian cancer: 1993 consensus statements. *Ann Oncol* 1993, **4**(Suppl. 4), 83–88.
6. Spencer CM, Faulds D. Paclitaxel: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the treatment of cancer. *Drugs* 1994, **48**(5), 794–847.
7. McGuire WP, Hoskins WJ, Brady MF, *et al.* Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. *N Engl J Med* 1996, **334**(1), 1–6.
8. Neijt JP. New therapy for ovarian cancer (editorial). *N Engl J Med* 1996, **334**(1), 50.
9. Doyle C, Stockler M, Pintilie M, Panesar P, Warde P, Sturgeon J, Oza AM. Resource implications of palliative chemotherapy for ovarian cancer. *J Clin Oncol* 1997, **15**, 1000–1007.
10. Covens A, Boucher S, Roche K, *et al.* Is paclitaxel and cisplatin a cost-effective first-line therapy for advanced ovarian carcinoma? *Cancer* 1996, **77**, 2086–2091.
11. McGuire W, Neugut AI, Arikian S, *et al.* Analysis of the cost-effectiveness of paclitaxel as alternative combination therapy for advanced ovarian cancer. *J Clin Oncol* 1997, **15**(2), 640–645.
12. Messori A, Trippoli S, Becagli P, Tendi E. Pharmacoeconomic profile of paclitaxel as a first-line treatment for patients with advanced ovarian carcinoma. *Cancer* 1996, **78**, 2366–2373.
13. Beck JR, Kassirer JP, Pauker SG. A convenient approximation of life expectance (the 'DEALE'). I. Validation of the method. *Am J Med* 1982, **73**(6), 883–888.

14. Tengs TO, Adams ME, Pliskin JS, *et al.* Five hundred life-saving interventions and their cost-effectiveness. *Risk Anal* 1995, **15**, 369–390.
15. Kievit J, van de Velde CJH. Utility and cost of carcinoembryonic antigen monitoring in colon cancer follow-up evaluation. A Markov analysis. *Cancer* 1990, **65**, 2580–2587.
16. Desch CE, Lasala MR, Smith TJ, *et al.* The optimal timing of autologous bone marrow transplantation in Hodgkin's disease patients following a chemotherapy relapse. *J Clin Oncol* 1992, **10**, 200–209.
17. Hillner BE, Smith TJ, Desche CE. Efficacy and cost-effectiveness of autologous bone marrow transplantation in metastatic breast cancer. *JAMA* 1992, **267**, 2055–2061.
18. Welch HG, Larson EB. Cost-effectiveness of bone marrow transplantation in acute nonlyphocytic leukemia. *N Engl J Med* 1989, **321**, 807–812.
19. Desch CE, Hillner BE, Smith TJ, *et al.* Should the elderly receive chemotherapy for node-negative breast cancer? *J Clin Oncol* 1993, **11**, 777–782.
20. Hillner BE, Smith TJ. Efficacy and cost-effectiveness adjuvant chemotherapy in woman with node-negative breast cancer. *N Eng J Med* 1991, **324**, 160–168.
21. Ozer H, Golomb HM, Zimmerman H, *et al.* Cost-benefit analysis of interferon alpha 2b in treatment of hairy cell leukemia. *J Natl Cancer Inst* 1989, **81**, 594–602.
22. Rees GJG. Cost-effectiveness in oncology. *Lancet* 1985, **2**, 1405–1408.
23. Eisenhauer EA, Bokkel Huinink WW, Swenerton KD, *et al.* European-Canadian randomized trial of paclitaxel in relapsed ovarian cancer: high-dose versus low-dose and long versus short infusion. *J Clin Oncol* 1994, **12**, 2654–2666.