Cost-Effectiveness of Second-Line Chemotherapy for Non-small Cell Lung Cancer

An Economic, Randomized, Prospective, Multicenter Phase III Trial Comparing Docetaxel and Pemetrexed: The GFPC 05-06 Study

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Background: There are few data on the cost-effectiveness of second-line chemotherapies for non-small cell lung cancer (NSCLC). The objective of this phase III, randomized, multicenter, prospective study was to compare the cost-effectiveness of docetaxel and pemetrexed, two widely used drugs.

Methods: We compared, from a payer's perspective, the directs costs and effectiveness of docetaxel (75 mg/m^2, arm A) and pemetrexed (500 mg/m^2, arm B) administered every 3 weeks to NSCLC patients who had progressed after first-line platinum-based chemotherapy. Monthly health utilities (based on disease states: responding, stable or progressive, and grade 3/4 toxicities) were derived from the literature. Costs were prospectively assessed.

Results: One hundred fifty patients were enrolled between February 2006 and June 2008. The patients in the docetaxel and pemetrexed arms had similar clinical characteristics and treatment efficacy (respective objective response rates 10.7% and 12%; median progression-free survival times 2.8 and 2.5 months; median survival times 8.0 and 6.4 months, respectively). Grade 3/4 toxicities were significantly less frequent with pemetrexed (52.0% versus 33.3%, $p = 0.02$). Docetaxel was associated with lower treatment-period costs (€9709 ± €6272 versus €13,436 ± €6508, $p < 0.001$). Docetaxel had a more favorable cost-utility ratio than pemetrexed. When compared with best supportive care, the cost-utility was €32,652/quality-adjusted life year for docetaxel and €40,980/quality-adjusted life year for pemetrexed.

Conclusion: Second-line treatment for NSCLC is more cost-effective with docetaxel than with pemetrexed. Both strategies have acceptable cost-effectiveness ratios compared with commonly used and reimbursed regimens for advanced NSCLC.

Key Words: Non-small cell lung cancer, Second-line chemotherapy, Pemetrexed, Docetaxel, Cost-effectiveness, Cost-utility.

(*J Thorac Oncol.* 2011;6: 161–168)

The National Institutes of Health estimated that $89 billion was spent on cancer care in the United States in 2007, and that the total economic burden reached $219.2 billion when indirect costs associated with lost productivity and death were taken into account. Recent trends suggest that the growth in cancer spending will accelerate, owing to costly new treatments and the increasing number of cancer patients. Lung cancer is the second most common malignancy in the United States and is the leading cause of cancer-related death.[1] Non-small cell lung cancers (NSCLC) represent 80% of lung cancers, and most patients already have advanced or metastatic disease at diagnosis. Combination chemotherapy is recommended for patients with good performance status.[2] Most patients progress after first-line therapy, and second-line chemotherapy is recommended for those whose performance status remains acceptable. Several agents have been shown to improve survival in this setting, including docetaxel and pemetrexed.[2–6] Docetaxel improves survival relative to best supportive care,[7] and pemetrexed showed similar efficacy but less toxicity when compared head-to-head with docetaxel in a phase III randomized trial involving 571 previously treated patients with advanced NSCLC.[8] The median and progression-free survival (PFS) times were, respec-

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Disclosure: The authors declare no conflicts of interest.

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Presented in part at the 2009 WCLC conference, San Francisco, CA.

A. Vergnenegre and C. Chouaid had full control of the study design, data analysis and interpretation, and manuscript preparation. All the authors were involved in planning the analysis and drafting the manuscript. The final draft manuscript was approved by all the authors.

The sponsors had no role in the study design, study realization, data analysis, or manuscript preparation. GFPC and Limoges University Hospital were the promoters and have the result property. The data were analyzed by the GFPC statistician and interpreted by the authors.

ISSN: 1556-0864/11/0601-0161

tively, 8.3 and 2.9 months with pemetrexed and 7.9 and 2.9 months with docetaxel. Pemetrexed was associated with significantly fewer grade 3/4 adverse events (AEs),[8] fewer hospital admissions for AEs, and fewer toxic deaths.[8]

However, very few data are available on the cost-effectiveness of these two drugs. All pharmacoeconomic studies published to date are retrospective and model-based.[9–12] A recent international expert panel has stated that "prospective pharmacoeconomic analysis of second-line treatment would be useful to inform clinical practice in this setting."[13]

The principal objective of this study was to compare the cost-effectiveness of second-line docetaxel and pemetrexed therapy in NSCLC patients. Secondary end points were the responses rates, PFS, overall survival, and survival without major clinical toxicity.

PATIENTS AND METHODS

Patient Selection and Clinical Evaluation

This phase III, randomized, prospective, multicenter study included patients aged 18 years and older, with at least one measurable lesion, histology-proven stage IIIb or IV NSCLC, good performance status (Eastern Cooperative Oncology Group score 0–2), and progressive disease after a single cisplatin-based chemotherapy regimen for metastatic disease; one previous additional neoadjuvant, adjuvant, or neoadjuvant plus adjuvant regimen was allowed. Patients with symptomatic brain metastasis; grade 3 or 4 peripheral neuropathy; weight loss of 10% or more during the previous 6 weeks; uncontrolled pleural effusion; upper vena cava syndrome; previous docetaxel or pemetrexed therapy; non-steroidal anti-inflammatory drug dependency; or altered hematologic, kidney, or hepatic function were excluded. The patients were randomized, after stratification for performance status (0–1 versus 2) and the number of metastatic sites (≤ 1 versus >1), to receive one dose every 21 days of either pemetrexed (500 mg/m^2 as a 10-minute intravenous infusion) plus vitamin B12 injections and oral folic acid supplementation or docetaxel (75 mg/m^2 as a 1-hour intravenous infusion). The protocol was approved by Limoges Hospital ethics committee.

Cycles were repeated until unacceptable toxicity or disease progression occurred, or until the patient or investigator requested treatment discontinuation. Granulocyte colony-stimulating factor (G-CSF) primary prophylaxis was not allowed, but G-CSF could be used to treat neutropenia or to prevent neutropenia in patients who had neutropenia during a previous cycle. Comprehensive baseline assessment included laboratory tests and imaging studies. Hematological analyses were performed weekly and blood chemistry analyses on days 1 and 8 of each cycle. Toxicity was rated before each cycle by using the National Cancer Institute Common Toxicity Criteria (CTC), version 2. Tumor size was measured every three cycles (in keeping with standard French practices in second-line settings) by an independent panel using RECIST criteria.

Economic Assessment

First resource consumption was assessed prospectively from the case report forms throughout second-line chemotherapy. This analysis included the chemotherapy drugs, supportive treatment (recombinant human erythropoietin, antiemetics, growth factors, antibiotics, management of adverse effects, etc.), hospitalization for any reason, and medical transport. All the volumes were collected and added together, but only grade 3/4 AE management costs were taken into account.

Second costs were derived from national tariffs for diagnosis-related groups and national fees for ambulatory care, provided by the French Ministry of Health and the national health insurer.[14,15] Volumes, unit prices, and tariff sources are shown in Table 1.

Third, during the treatment period, all the data were prospectively recorded. Costs incurred after the period of second-line chemotherapy (remission period or disease progression period) were derived from a representative French nationwide sample of 428 patients, using chart review to assess the mean direct monthly cost of the first 18 months of NSCLC patient management.[16] Specifically, the costs included outpatient and inpatient services, care provision at skilled nursing facilities, outpatient and inpatient drugs and other medications, nursing care organization, home health visits (including medications), and durable medical equipment. Assuming a yearly increment of 3%, 1 month of management costs €217 (2009 values) during the remission phase and €2324 (2009 values) during the terminal phase.

Utility (Quality of Life) Assessment

Health state preference scores or utilities measure the strength of an individual's preferences for specific outcomes under conditions of uncertainty and are used to measure health-related quality of life (HRQL). After randomization, each patient was classified in one of the following mutually exclusive and exhaustive states each month: responding on chemotherapy, with or without grade 3/4 AEs; stable, with or without grade 3/4 AE; progression, with or without grade 3/4 AE; and death. The utilities were derived from UK society-based utility values for different stages of NSCLC and different grade 3/4 toxicities commonly associated with chemotherapy (Table 2).[17] Thus, we calculated the quality-adjusted life year (QALY) value per patient, from randomization to death or censor date, and QALY per treatment arm.

Costs of survival and utility were used to calculate, for each chemotherapy arm, a cost per life year ratio and a cost per QALY and to compare the values thus obtained between the two arms.

Sensitivity Analyses

The uncertainty and robustness of the model were evaluated in one-way sensitivity analyses, by varying the cost of chemotherapy and the values of utilities, the percentage of AEs hospitalization, and the percentage of patients treated by G-CSF while keeping the other parameters constant, over a range of likely values derived from confidence intervals or reasonable ranges.

TABLE 1. Description of Some Recorded Data for Economical Analysis, with Unit Price and Tariff Sources

Categories	Volumes	Unit Price	Origin
Transportation	Car	€11.73[a] + €0.83 per km	
	Ambulance	€49.33[a] + €2.12 per km	
Chemotherapeutic drugs	Docetaxel	€10.7/mg	Health Ministry[15]
	Pemetrexed	€2.9/mg	
Granulocyte colony-stimulating factor	Lenograstim and filgrastim	€115 and €119 per injection	Health Ministry[15]
Procedures	Chest X-ray	€21.28	16th version[14]
	Chest CT scan	€25.27	
	Lung scintigraphy	€176.85	
	Bronchoscopy	€86	
	Dorsal spine MRI	€69	
	Brain CT scan	€25.27	
	Brain MRI	€69	
Drug administration[b]	Outpatient	€417.00	DRG 10th version[15]
	Inpatient 1 night	€588.00	
	Inpatient 2 nights	€1809.00	
Follow-up[b]	Outpatient	€588.00	DRG 10th version[15]
Adverse event admission[b] (examples)	Poor performance status	€4158.21	DRG 10th version[15]
	Neutropenia/anemia	€3930.08	
	Breathlessness	€3450.43	
	Fever	€4015.61	
	Dehydration	€3563.22	
	Transfusion (outpatient)	€668.54	
Consultation	Ambulatory	€23.00	16th version[14]

[a] Average of four French areas.
[b] Average of 2006, 2007, and 2008 tariffs.
MRI, magnetic resonance imaging; CT, computed tomography; DRG, Diagnosis-related Groups.

TABLE 2. NSCLC Patients Treated with Second-Line Chemotherapies: Utility Values for Health States After Randomization (Derived from Nafees et al.[17])

Health State	Values
Responding without grade 3/4 toxicities	0.712
Responding with grade 3/4 toxicities	0.666
Stable without grade 3/4 toxicities	0.626
Stable with grade 3/4 toxicities	0.580
Progressive without grade 3/4 toxicities	0.473
Progressive with grade 3/4 toxicities	0.460

NSCLC, non-small cell lung cancer.

Statistical Analysis

The required number of patients was determined from published data, with a type 1 risk of 5% and a power of $1 - \beta$ at 80%. The number of patients required to show a 10% cost difference favoring one or other strategy was 72 per arm or a total of 150 patients when probable losses to follow-up were taken into account. Tumor response rates and the frequency of AEs were compared between the arms by using Fisher's exact test. All the responses were evaluated by an investigator panel. Quantitative variables were compared using Student's *t* test or the Wilcoxon test when the data were not normally distributed. The Kaplan-Meier and Cox methods were used for time-to-event analyses. Overall survival was censored at the date of the last follow-up visit for patients who were still alive. We also calculated survival without the most clinically important grade 3/4 toxicities (neutropenia lasting more than 5 days; febrile neutropenia; and documented infections related to neutropenia, anemia, thrombocytopenia, fatigue, nausea, vomiting, diarrhea, stomatitis, and neurosensory events), which is defined as the time from randomization to the first grade 3 or 4 toxicity or death.[18] Costs were estimated using nonparametric bootstrap methods (10,000 bootstrap resamples were generated). SAS software version 9 (SAS Inc., Cary NC) and Epi-Info V6.04 (CDC, Atlanta, GA) were used for statistical analyses.

RESULTS

Between February 2006 and June 2008, 150 patients recruited in 27 centers were randomized to receive pemetrexed every 3 weeks plus vitamin B12, 1000 μg every 9 weeks and folinic acid, 0.4 mg daily ($n = 75$), or docetaxel every 3 weeks ($n = 75$). The censor date was August 31, 2009. Figure 1 shows the study flow chart. Baseline characteristics were similar and well balanced across the treatment

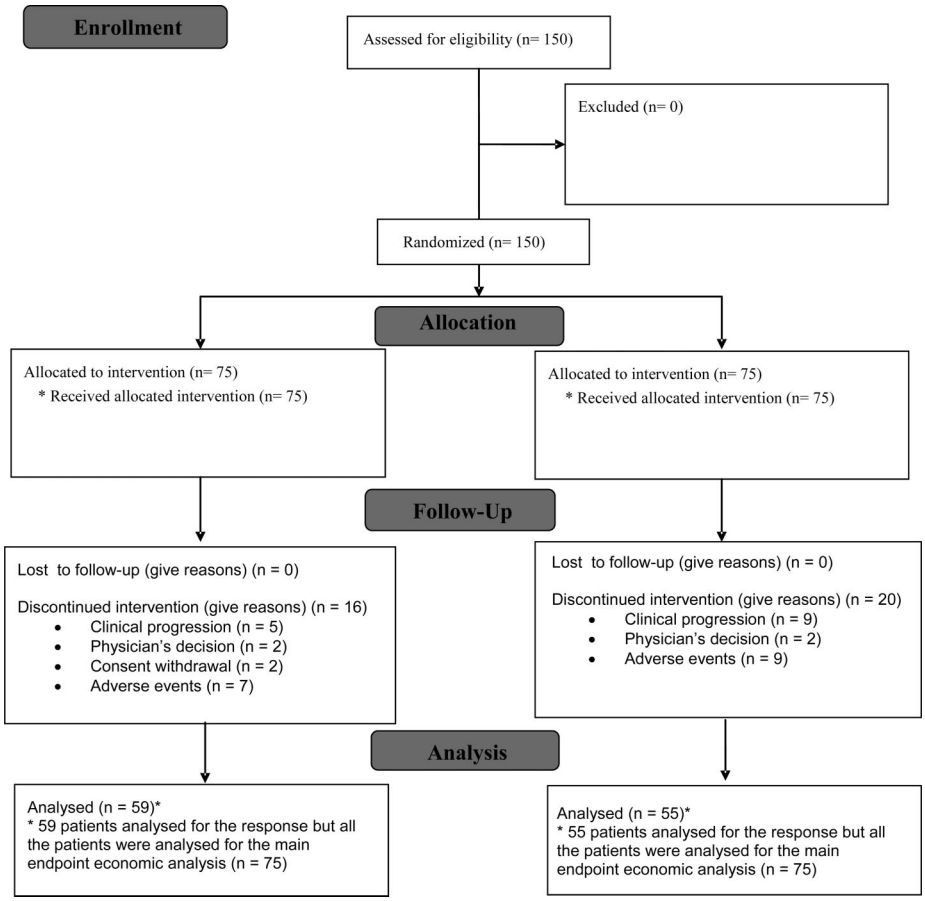

FIGURE 1. Study flow chart.

arms, with no statistically significant differences in age, gender, performance status, the proportion of stage IV disease, or histology (Table 3). There was no difference in the time between the end of first-line chemotherapy and the beginning of second-line chemotherapy (5.8 ± 6.1 months in the docetaxel arm and 5.1 ± 5.9 months in the pemetrexed arm). On average, the patients received 3.7 ± 1.9 cycles of docetaxel (range, 1–6 cycles) and 3.6 ± 1.8 cycles of pemetrexed (range, 1–7 cycles), with no difference in dose intensity (data not shown). Efficacy was similar in the two arms, with no significant difference in the tumor response rate or the PFS time (Table 3). The median overall survival time was also similar (8.0 months with docetaxel and 6.4 months with pemetrexed), and the 1- and 2-year overall survival rates were, respectively, 32.0% and 11.7% with docetaxel and 27.1% and 9.8% with pemetrexed (Figure 2). Patients treated with pemetrexed had significantly fewer episodes of thrombocytopenia, hair loss, and nausea of CTC grade 1/2 (data not shown) and significantly fewer CTC grade 3/4 toxicities ($p = 0.02$), including less neutropenia (34.7% and 8.0%, $p = 0.001$, with docetaxel and pemetrexed, respectively; Table 4). There was no difference in the frequency of hospitalization for AEs (0.44 ± 0.84 versus 0.52 ± 0.89 hospital admissions per patient with docetaxel and pemetrexed, respectively). Patients treated with docetaxel required significantly more supportive care (G-CSF, red cell transfusions, and recombinant human erythropoietin) than patients treated with pemetrexed (19.2% versus 2.6%, $p = 0.001$). There was no difference in the median survival time without selected grade 3/4 toxicities or death (2.7 and 3.5 months with docetaxel and pemetrexed, respectively; Figure 3). There was also no difference in QALY (Table 5). Docetaxel therapy was significantly less costly during the treatment periods (€9709 ± €6272 versus €13,436 ± €6508, $p = 0.001$) and during the overall study period (€13,714 ± €7387 versus €16,802 ± €7852 [2009 values], $p = 0.022$). Docetaxel was dominant versus pemetrexed with an average total cost difference of €−3,182 (€−5,158; €−1096) and an average utility difference of 0.14 (−1.34; 1.63). Figure 4 shows the distribution of the two values according to the bootstrap simulation. When compared with best supportive care, the costs per life year and per QALY were significantly lower in the docetaxel arm (€15,545 versus €22,798, $p < 0.01$, and €32,652 versus €40,980, $p = 0.003$).

Sensitivity analyses (Table 6) showed that the cost of pemetrexed therapy would have to fall by 30% to balance the QALY values in the two arms. Varying the rate of G-CSF administration in the docetaxel arm, the rate of hospitalization (according to the results of Hanna et al.,[8] 23.9% for docetaxel and 7.9% for pemetrexed) or utility values by ±10% did not affect the results.

TABLE 3. Patient Characteristics and Efficacy of Docetaxel and Pemetrexed

Patients' Characteristics	Docetaxel: Arm A (n = 75)	Pemetrexed: Arm B (n = 75)
Median age (yr, 95% CI)	59.4 ± 8.3	58.3 ± 8.7
Gender (male, %)	64 (85.3%)	62 (82.7%)
ECOG PS (0 or 1, %)	70 (93.3%)	71 (94.7%)
Stage IV (n, %)	59 (78.7%)	62 (82.7%)
Histology		
Squamous (n, %)	23 (30.7%)	18 (24%)
Nonsquamous (n, %)	52 (69.3%)	57 (76%)
Time since first-line chemotherapy (mo, ±SD)	5.8 ± 6.1	5.1 ± 5.9
≤3 mo (%)	50%	45%
Mean cycles of first-line chemotherapy (±SD)	4.5 ± 2.5	4.4 ± 2.1
Mean cycles of second-line chemotherapy (±SD)	3.7 ± 1.9	3.6 ± 1.8
Response rates		
Not assessable	16 (21.3%)	20 (26.7%)
Progressive disease	30 (40%)	26 (34.6%)
Stable disease	21 (28%)	20 (26.7%)
Objective response	8 (10.7%)	9 (12%)
PFS (mo, 95% CI)	2.8 (2.2–4.2)	2.5 (2.1–3.9)
Median survival (mo, range)	8 (5.12–10.4)	6.4 (4.8–8.4)
1-yr survival (%, ±SD)	32 ± 5	27.1 ± 5.2
2-yr survival (%, ±SD)	11.7 ± 4	9.8 ± 3.6

ECOG PS, Eastern Cooperative Oncology Group performance status; CI, confidence interval; PFS, progression-free survival.

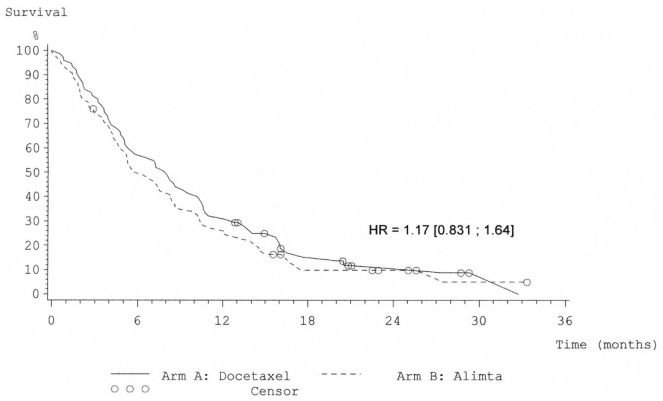

FIGURE 2. Overall survival in the two arms.

DISCUSSION

In this randomized, multicenter, prospective study comparing the cost-effectiveness of docetaxel and pemetrexed, two second-line chemotherapies widely used for NSCLC, efficacy was similar with the two drugs, but pemetrexed was associated with significantly less overall grade 3/4 toxicity. Compared with pemetrexed, docetaxel was associated with significantly lower treatment-period costs and total management costs and a better ratio of cost per QALY (€32,652 versus €40,980, $p = 0.003$). In terms of efficacy and toxicity, the results of this study are similar to those published elsewhere. In the pivotal study comparing docetaxel with best supportive care,[7] median overall survival was 7.0 months and the 1-year survival rate was 29%, compared with 8 months and 32% in our study. Likewise, the 1-year survival rate in the docetaxel arm of the TAX320 trial was 32%.[19] Neutropenia and febrile neutropenia were the main toxicities reported in this trial. Pemetrexed 500 mg/m^2 was compared with docetaxel 75 mg/m^2 in a phase III face-to-face trial.[8] The response rate, PFS, median overall survival, and 1-year survival with docetaxel and pemetrexed were, respectively, 8.8% and 9.1%, 2.9 and 2.9 months, 7.9 and 8.3 months, and 29.7% in both arms. As in our study, patients receiving docetaxel experienced significantly higher rates of neutropenia, severe neutropenia, and febrile neutropenia. Finally, in a recent review of phase III trials of second-line NSCLC chemotherapy,[5] the median objective response rate was 6.8% and the median overall survival time was 6.6 months—values very similar to those observed in our study.

Patients who experience disease progression during or after first-line treatment for advanced NSCLC have limited life expectancy.[5] Quality of life is often compromised by disease-related symptoms, residual toxicity of prior chemotherapy, and comorbidity. Second-line treatment should provide symptom palliation, optimize quality of life, and increase survival.

There are few published data on quality of life or utilities associated with second-line NSCLC chemotherapies. Pujol et al.[18] retrospectively compared the time from randomization to the first occurrence of most clinically important grade 3/4 toxicities or death in the prospective phase III study comparing pemetrexed and docetaxel.[8] As in our study, patients treated with pemetrexed had significantly fewer CTC grade 3/4 toxicities ($p = 0.001$). The median survival times and 6-month survival rates without grade 3/4 toxicity in patients treated with pemetrexed and docetaxel were, respectively, 3.5 and 2.7 months and 25.7% and 10.1%. The respective 12-month survival rates without grade 3/4 toxicity were 15.9% and 11.4%. Regarding the burden of NSCLC on HRQL, little information is available on the preferences of patients or society with respect to disease states.[20–23] Trippoli et al.,[24] reporting utility and HRQL data (based on the SF-36 and EQ-5D questionnaires) for 95 NSCLC patients, showed that HRQL was significantly worse in patients with metastatic NSCLC. We used the results of Nafees et al.,[17] who adapted existing health state descriptions in metastatic breast cancer, to describe our patients receiving second-line treatment for NSCLC. Each health state describes the symptom burden of disease and its impact on different functions. The disutility related to each disease state and to toxicity was estimated and combined to obtain health state values. There are also few published studies on second-line treatment costs in advanced NSCLC. Available pharmacoeconomic studies are based on retrospective models and have several limitations. Using data from the pivotal study comparing docetaxel and best supportive care (BSC) from the perspective of the Canadian public healthcare system, limited to direct medical costs, Leighl et al.[9] found an incremental survival benefit of 2 months over

TABLE 4. Grade 3 and 4 Toxicities in the Two Arms

	Docetaxel (n = 75)		Pemetrexed (n = 75)		
Grade 3 and 4 Toxicities	**No. of Events**	**No. of Patients (%)**	**No. of Events**	**No. of Patients (%)**	***p***
Neutropenia	45	26 (34.7)	16	6 (8)	<0.001
Thrombocytopenia	1	1 (1.3)	5	5 (6.7)	NS
Anemia	1	1 (1.3)	9	5 (6.7)	NS
Infection	5	4 (5.3)	3	3 (4)	NS
Renal toxicity	—	—	1	1 (1.3)	NS
Hepatic toxicity	3	2 (2.7)	9	1 (1.3)	NS
Fatigue	19	12 (16)	8	6 (8)	NS
Hair loss	10	4 (5.3)	—	—	
Peripheral neuropathy	2	2 (2.7)	2	1 (1.3)	NS
Nausea—vomiting	2	2 (2.7)	3	2 (2.7)	NS
Pain	7	6 (8)	6	4 (5.3)	NS
Other	4	3 (4)	2	2 (2.7)	NS
Total	99	39 (52)	64	25 (33.3)	0.02

χ^2 test or Fisher's exact test.

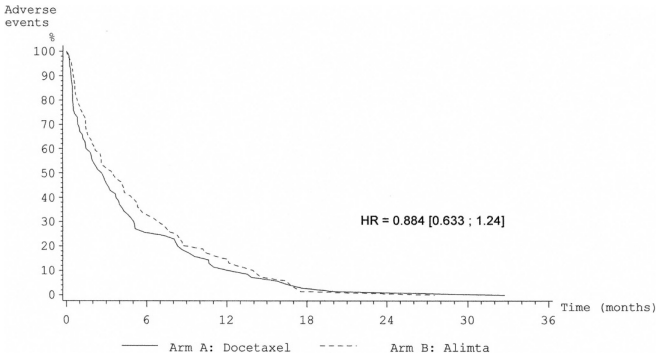

FIGURE 3. Survival without grade 3/4 adverse events and death.

TABLE 5. Costs (2009 Euros) and Cost-Effectiveness of Docetaxel and Pemetrexed

	Docetaxel (n = 75)	**Pemetrexed (n = 75)**	***p***
Costs (2009 euros)			
Treatment periods (drugs, administration, transportation, and adverse events)	9709 ± 6272	13,436 ± 6508	<0.001
Follow-up	782 ± 1568	731 ± 1512	NS
Palliative care	3223 ± 3479	2634 ± 3227	NS
Total	€13,714 ± €7387	€16,802 ± €7852	0.022
QALY	0.42 ± 0.4	0.41 ± 0.39	NS
Cost-effectiveness			
Cost per LYG	15,545	22,798	<0.01
Cost per QALY	32,652	40,980	0.003

LYG, life year gained; QALY, quality-adjusted life years.

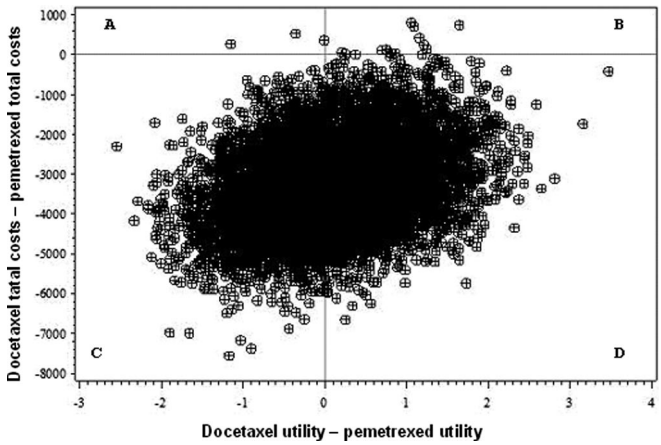

FIGURE 4. Bootstrap of cost and utility differences (*A* and *B* areas in favor of pemetrexed, *C* and *D* areas in favor of docetaxel). The results favored docetaxel arm.

TABLE 6. Sensitivity Analysis

	Cost per QALY		
Variable	**Docetaxel (n = 75)**	**Pemetrexed (n = 75)**	***p***
Cost of pemetrexed: −30%	32,913	34,403	NS
Rate of G-CSF use in docetaxel arm (50%)	34,218	40,980	<0.001
Hospitalization rates from the study by Hanna et al.[8]	39,790	45,588	<0.01
Values of utilities: −10%	36,570	45,823	<0.001
Values of utilities: +10%	29,921	37,407	<0.001

QALY, quality-adjusted life years; G-CSF, granulocyte colony-stimulating factor.

BSC and an incremental cost-effectiveness of docetaxel of CaD $31,776 (1999 values) per life year gained (LYG) versus BSC. This cost-effectiveness was most sensitive to changes in mean survival (−20%) and ranged from CaD $18,374 to 117,434 per LYG. Using data from the same randomized trial, and focusing on direct medical costs limited to drug acquisition and administration, Holmes et al.[10] found that,

from the perspective of the UK National Health Service, the use of docetaxel resulted in a survival benefit of 3.8 months with a cost-effectiveness of £13,863 per LYG (2000–2001 values). However, this study did not consider AEs or quality of life, which were drivers of both QALY and costs in our analysis. Pavlakis et al.[12] assessed the cost-effectiveness of pemetrexed relative to docetaxel. Rather than focusing on direct medical costs, they chose the reduction in toxicity-related hospitalization as the outcome measure. The incremental cost of avoiding one toxicity-related hospital admission was US $15,754 (year of value not stated), suggesting an advantage of pemetrexed.

Our results are in line with those of a recently published model-based analysis comparing the economic value of docetaxel, pemetrexed, and erlotinib in a cohort of patients with refractory advanced-stage NSCLC.[25] The authors developed a decision analytic model to evaluate, from the US payer's perspective, the incremental costs and QALY of these three strategies, based on efficacy and AE rates in published clinical trials, as well as the work of Nafees et al. on utilities and on publicly available cost sources. They found that treatment with erlotinib, docetaxel, and pemetrexed yielded 0.42, 0.41, and 0.41 QALY, compared with 0.42 ± 0.4 and 0.41 ± 0.39, respectively, for docetaxel and pemetrexed in our study. Total costs were US $37,000, 39,100, and 43,800 for erlotinib, docetaxel, and pemetrexed, respectively, compared with €13,714 ± €7387 and €16,802 ± €7852, respectively, for docetaxel and pemetrexed in our study. The costs of periods of progression were markedly different: US $24,017 for the three strategies in the study by Carlson et al.,[25] compared with €3223 ± €3479 and €2634 ± €3227, respectively, for docetaxel and pemetrexed in our study. In Carlson's model-based study,[25] one-way sensitivity analyses indicated that the primary drivers of variations in total costs were the time spent in the progression-free health state, the treatment duration, and drug costs. The primary driver of the QALY difference was the time spent in the progression-free health state.

Our study has certain limitations. First, costs were identified prospectively only during the active treatment periods, whereas management costs after the end of chemotherapy were derived from a national database. Second, our analysis was limited to direct lung cancer-related medical costs: indirect costs such as lost productivity and caregiver costs were not included. Third, the expression of utilities reflects the value from the point of view of society rather than that of the patients concerned. Finally, we did not analyze the cost-effectiveness of erlotinib, an oral epidermal growth factor receptor tyrosine kinase inhibitor that has been shown to improve survival among patients with advanced NSCLC who have previously received one or more chemotherapy regimens.[26,27] Several recent model-based pharmacoeconomic studies[25,28] suggest that erlotinib 150 mg/d is a cost-saving second-line option relative to approved second-line intravenous chemotherapies such as docetaxel and pemetrexed.

CONCLUSION

Second-line NSCLC chemotherapy is more cost-effective with docetaxel than with pemetrexed, when they are directly compared. A head-to-head prospective trial is now needed to compare the cost-effectiveness of these chemotherapies and erlotinib.

APPENDIX: THE GFPC 0506 TEAM

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ACKNOWLEDGMENTS

Supported by an unrestricted educational grant from Sanofi-Aventis and Amgen. Administrative support was provided by Direction de la Recherche Clinique (Limoges University Hospital).

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