ELSEVIER

Lung Cancer 14 (1996) 31–44

LUNG CANCER

IASLC

Cost analysis of hospital treatment — two chemotherapic regimens for non-surgical non-small cell lung cancer

A. Vergnenègre*[a], M. Perol[b], E. Pham[c], the GFPC (Groupe Français Pneumo Cancérologie)[1]

[a]*Service de Pneumologie, Hôpital Universitaire du Cluzeau, 87042 Limoges cedex, France*
[b]*Service de Pneumologie, Hôpital de la Croix Rousse, Lyon, France*
[c]*Laboratoire de Biostatistiques, Faculté de Médecine Alexis Carrel, Lyon, France*

Received 12 June 1995; revision received 16 October 1995; accepted 24 October 1995

Abstract

Study objectives: compare the costs of two regimens of chemotherapy. Apply weighted costs to an economic model in a hospital perspective. Design: prospective randomized study of two groups of patients receiving: branch B, mitomycin-navelbine-cisplatin (MNP); branch A, mitomycin-vindesine-cisplatin (MVP). Setting: pneumologic units of University and non-University hospitals. Methods: clinical evaluation during chemotherapy incorporated events enabling construction of an event tree. Direct hospital costs included those of: cytostatic agents, materials used and nursing time; costs of side-effects (medical and paramedical time, diagnostic and therapeutic examinations). Effectiveness was measured in terms of response rates. Patients: 209 patients were included, 100 in arm B, 109 in arm A. Results: the response rates were 25% in branch B, 17% in branch A. In the hypothesis of equivalence of the two strategies, we compared only overall mean cost per patient. Despite the fact arm B needed more hospital injections, the difference was low (+4.6%). For a difference in effectiveness, the opposite was observed for the average cost-effectiveness ratio: arm B was less costly (−12 339.40 FF for a responder). Conclusion: incorporation of economic parameters was found to have a bearing on the choice of chemotherapeutic regimen for the treatment of non-small cell lung cancer. Economic analyses of this kind can provide useful extra information for rational therapeutic decisions.

* Corresponding author.

[1] P. Balmes (Nîmes), F. Blanchon (Meaux), F. Bonnaud (Limoges), P. Carles (Toulouse), J. Clavier (Brest), J.C. Guérin (Lyon), J.P. Kleisbauer (Marseille), J.F. Muir, D. Paillotin (Rouen), R. Poirier (Aix), A. Taytard (Bordeaux).

0169-5002/96/$15.00
SSDI 0169-5002(95)00511-0

Keywords: Lung cancer; Chemotherapy; Costs analysis; Cost-effectiveness

1. Introduction

The development of medical decision analysis has stemmed largely from difficulties in choosing optimum strategies in the face of the continuing advances in diagnostic and therapeutic techniques [4]. Costs analysis is increasingly justified in parts of medicine employing expensive treatments whose benefits over existing methods may not be immediately apparent. It raises ethical issues concerning the cost of a new procedure with respect to its effectiveness. Specific models are required to identify such factors [4,17]. In certain branches of medicine such as lung cancer, there have been relatively few economic studies, although there are reports on the costs of different management strategies [3,16], hospital admission [13] and various therapeutic strategies [10].

For non-surgical non-small cell lung cancers, the results of chemotherapy vary according to the studies [2,14,15,20]. The response rates range from 20–50%, but complete response rates rarely exceed 3–5% [1,18]. New agents are continually being introduced in chemotherapeutic protocols, and the current most effective molecules in single drug regimens are vinca-alkaloids, ifosfamide, cisplatin, mitomycin and etoposide [1,7]. A new molecule, navelbine, has been reported to be efficient in both single drug [5] and multiple drug regimens [11].

The GFPC (Groupe Français de Pneumo-Cancérologie) has compared the efficacy of navelbine in combination with cisplatin-mitomycin (MNP) against the combination, cisplatin-mitomycin-vindesine (MVP) in a randomized trial [12]. The response rates were 25% (CI 95%:17–32) for MNP, 17% (10–24) for MVP. In stage III patients, the results were comparable 27.5% (MNP) and 25.4% (MVP) while, in stage IV patients, there was a difference in the results: 20% for MNP, 6% for MVP. However, navelbine is a relatively expensive drug for hospital pharmacies and its mode of administration (weekly) involves a large number of injections (for both in-patients and out-patients). Since cost-effectiveness analysis is increasingly entering medical practice including oncology [6,8], we decided to include economic parameters in the design of a clinical trial.

The aims of the study were: to evaluate the direct hospital costs of two therapeutic strategies (cost of drugs and consumables, cost of chemotherapic administration and cost of side-effects), to determine the optimum strategy in an economic perspective.

2. Materials and methods

2.1. Population

The patients recruited from the various participating centers received three courses of the following two combinations in a center randomized design: branch B, cisplatin 120 mg/m^2 on day 1, day 29, day 71 — mitomycin 8 mg/m^2 on day 1, day 29, day 71 — navelbine 25 mg/m^2/week for 16 weeks, vs. the combination of

branch A, cisplatin 120 mg/m^2 on day 1, day 29, day71 — mitomycin 8 mg/m^2 on day 1, day 29, day 71 — vindesine 3 mg/m^2 on day 1, day 8, day 15, day 22, day 29 then every fortnight.

The inclusion criteria were: non-surgical non-small cell lung cancer in stages III or IV without previous treatment and in the absence of cerebral metastases in patients under 75 years of age with a performance status ≤ 2. All patients gave their informed consent and the protocol was approved by an Ethics Committee. Survival and toxicity were analyzed for all patients included in the trial. Response to treatment was evaluated from the results of chest X-ray, CT-scan and endoscopic examinations by a panel of expert observers. Tumor type was verified by a panel of histologists.

2.2. Calculation of costs

We only recorded direct costs in our hospital perspective: the cost of chemotherapy and the cost of side-effects (according to WHO grades) requiring hospital treatment.

For each phase, the following costs were taken into account: (1) time spent by medical and paramedical personnel expressed in minutes. The personnel recorded the time spent in preparation and administration of the cytostatic agents. For the side-effects, the mean time spent per day per patient by the medical and paramedical personnel was recorded. The overall cost was calculated from mean salary scales of hospital staff in each grade (in terms of gross 1993 earnings). (2) Drugs and consumables: the cost of cytostatics was the average cost of the various formulations. It was expressed as the total dose received by all the patients in each branch. There was no difference in the body surface area between the two branches. (3) Investigations and laboratory tests: the scales used by the French Social Security System were employed for the complementary investigations with the following prices in 1993 for the corresponding letter codes: biological procedures, B = 1.65 FF, radiological procedures, Z = 10.35 FF, other investigations, K = 12.40 FF.

We recorded the volume of medical, para-medical time spent, the amounts of pharmaceutical and material quantities consumed per patient in each center. Prices were recorded on the data from two centers: a small University Hospital (Limoges) and a large University Hospital (Lyon), according to the methodology of a Canadian study [10].

2.3. Measurement of effectiveness

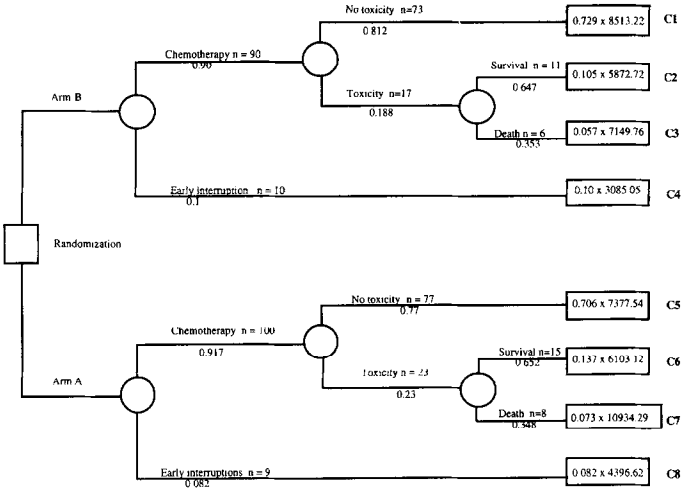
The study was performed during the administration of chemotherapy (16 weeks). The criteria of effectiveness we employed was the number of patients showing an objective response with respect to either of the number of patients included. In many studies, effectiveness is expressed in QALY (Quality Adjusted Life Years). We only recorded costs during the treatment period and not over the follow-up period. In accordance with the objective of the study, a criterion of effectiveness was chosen for this shorter period.

3. Results

3.1. Population

From September 1990 to May 1992, 209 patients were analyzed in this study: 109 in branch A and 100 in branch B. They included 199 men (95%) and 10 women (5%) of mean age 60.7 years (range 33–74 years), with 40% in stage IV, 42% in stage IIIB, and 18% in stage IIIA. The tumors fell into the following histological types: 63% epidermoid carcinomas, 25% adenocarcinomas, 12% undifferentiated large cell cancers.

The two groups were comparable in age, gender, performance status, stage, histological type. Patients receiving the full course of chemotherapy were 73% in branch B and 71% in branch A. The overall objective response rate was 25% in branch B, and 17% in branch A. For the evaluable patients, the response rates rose to 34.2% in branch B, and 23.4% in branch A. The differences for response rates between the two branches in the whole sample were not statistically significant ($P = 0.15$). The response rates were similar for stage III patients (27.5% in branch B, 25.4% in branch A). There were greater differences for stage IV patients (20% in branch B, 6% in branch A).



The first number in the rectangle is the product of the observed probabilities, the second number is the overall cost per patient of the branch according to :

C1: three complete courses of chemotherapy for branch B (MNP)
C2: interrupted chemotherapy due to a side effect with patient's survival for branch B
C3: interrupted chemotherapy due to a side effect with patient's death for branch B
C4: early interruption of chemotherapy not in relation to a side effect for branch B

Calculation is similar for branch A: C5, C6, C7, C8.

Fig. 1. Representation of the event tree taking account of random events in the two chemotherapeutic regimens analyzed. Branch B: mitomycin-navelbine-cisplatin (MNP), branch A: mitomycin-vindesine-cisplatin (MVP). The coefficient inside the end rectangle is the product of the different random elements in each branch. Example: $0.729 = 0.811 \times 0.9$. This is then multiplied by the average direct cost per patient in each branch. It is possible to get an average cost per patient and per branch (which is given in Table 4).

In branch B, 10 patients dropped out during the trial (10%) versus 9 in branch A (8.2%). Drop out was defined as either withdrawal of treatment or cases lost to follow-up with no imputation to toxicity of the cytostatic agents. For those receiving the complete course of chemotherapy, 17 cases of toxicity (17/90: 18.8%) were observed in group B with 6 deaths and 11 survivors. In group A, there were 23 cases of toxicity (23/100: 23%) with 8 deaths and 15 survivors. Toxicity was classified according to the WHO criteria, but we only recorded toxicities, which led to admission to hospital.

These events could be represented on a tree (Fig. 1). The first node is the treatment decision with the random split of the population into the two treatment groups. All the other nodes were hazard nodes [11]. The percentages shown in the diagram correspond to the frequencies from the observed data. A coefficient could be calculated by multiplying the different probabilities for each branch. This coefficient is then multiplied by the cost.

Table 1
Calculated cost of one side-effect according to branch and outcome

	Branch B			Branch A			
	N	No. of days in hospital	Cost (FF)	N	No. of days in hospital	Cost (FF)	Calculated cost (FF)
Side effects without death							
Hematologic	2	11	6949.76	2	25	15 372.17	5580.48
Digestive	1	0	0.00	1	1	502.71	251.35
Renal	2	10	5541.61	2	13	5240.31	2695.48
Hearing	1	7	1994.74	1	7	1897.64	1946.19
Cardiac	1	2	2661.88	1	8	3127.00	2894.44
Peripheral nerves	3	12	11 219.27	6	21	9184.9	2266.02
Central nervous system	—	—	—	1	7	3337.15	3337.15
Pneumologic	—	—	—	1	1	372.00	372.00
Side effects with death							
Hematologic	4	13	5960.64	4	37	26 363.68	4040.54
Digestive	—	—	—	3	25	23 109.35	7703.11
Renal	—	—	—	1	34	10 428.86	10 428.86
Hearing	—	—	—	—	—	—	—
Cardiac	1	20	6040.46	—	—	—	6040.65
Peripheral nerves	—	—	—	—	—	—	—
Central nervous system	—	—	—	—	—	—	—
Pneumologic	1	2	3706.27	—	—	—	3706.27

For each side-effect, the cost is calculated as shown in appendix 1. The side-effects are then grouped per branch and outcome (survival or death).

The average costs of the two branches were calculated in an attempt to avoid bias from the larger number of days prior to death, which would penalize one of the branches in the cost calculations.

No., number; FF, French francs; N, number of patients.

3.2. Costs

Direct costs were calculated for each branch of the tree. The distribution of the patients in each event can influence the costs. We use the event tree to weight the recorded costs. This method was used in an attempt to reduce bias between the two strategies (Fig. 1).

For the side-effects, the calculation is shown in appendix 1. This gave the cost of the side-effects for each branch in survivors and non-survivors. Their values are given in Table 1. There were some variations with the number of days of hospital care and the treatments between the two branches. Some patients in branch A who died from side-effects had longer stays in hospital giving rise to a higher cost. The patients in the other branch who died sooner produced a lower cost for the same side-effect. To avoid this bias, we have calculated an average cost for each type of side-effect, according to the outcome (death or survival).

Table 2
Cost of chemotherapy (drugs, consumables and time spent) for in-patients

Hospitalisation	Unit price	Costs
Nursing time		
Time for the preparation of products (25 min)	1.89 FF	47.25 FF
Monitoring infusion (60 min)	1.89 FF	113.4 FF
Materials		
Physiological solution (750 ml)	0.01 FF	6.97 FF
Glucose solution	0.01 FF	33.71 FF
Mannitol (500 ml)	0.02 FF	9.1 FF
Perfusors ($n = 3$)	3.7 FF	11.1 FF
Catheter (10 mm)	3.4 FF	3.4 FF
Syringes plastipak (30 ml, $n = 3$)	1.92 FF	5.76 FF
Syringes (20 ml, $n = 4$)	0.45 FF	1.8 FF
Solvent for injectable drug ($n = 4$)	2.05 FF	8.2 FF
Needles teruno (1.2 × 40, $n = 7$)	0.11 FF	0.77 FF
Compresses (4 × 4 $n = 4$)	0.93 FF	3.72 FF
Total		245.18 FF

Drugs	Unit price	Average price
Cisplatine (10 mg)	1.7 FF	1.38 FF
Cisplatine (25 mg)	1.28 FF	1.38 FF
Cisplatine (50 mg)	1.16 FF	1.38 FF
Mitomycine (2 mg)	8.2 FF	7.83 FF
Mitomycine (10 mg)	7.46 FF	7.83 FF
Vindesin (1 mg)	143.3 FF	131.62 FF
Vindesin (4 mg)	119.43 FF	131.62 FF
Navelbine (10 mg)	13.00 FF	12.30 FF
Navelbine (50 mg)	11.60 FF	12.30 FF

Table 3
Cost of chemotherapy (consumables, drugs and time spent) for ambulatory patients

Ambulatory patient	Unit price	Costs
Nursing time		
Preparation, monitoring infusion (45 min)	1.89 FF	85.05 FF
Materials		
Perfusor ($n = 2$)	3.7 FF	5.4 FF
Glucose solution (250 ml)	0.01 FF	2.32 FF
Catheter (10 mm)	3.4 FF	3.4 FF
Syringes plastipak (30 ml, $n = 1$)	1.92 FF	1.92 FF
Syringes (20 ml, $n = 1$)	0.45 FF	0.45 FF
Solvent for dilution	2.05 FF	2.05 FF
Compresses (4×4, $n = 4$)	0.93 FF	3.72 FF
Total		104.31 FF
Products	**Unit price**	**Average price**
Vindesin (1 mg)	143.30 FF	131.62 FF
Vindesin (4 mg)	119.43 FF	131.62 FF
Navelbine (10 mg)	13.00 FF	12.30 FF
Navelbine (50 mg)	11.60 FF	12.30 FF

Tables 2 and 3 show the cost of the cytostatic agents along with the materials required and the nursing time. Out-patients were distinguished from the in-patients as less nursing time was required for these patients.

Appendix 2 shows an example of the calculation for the C1 branch (administration of all courses of treatment) and C2 branch (chemotherapy with side-effect and

Table 4
Average costs per patient

Branch tree	Branch B		Branch A	
	N	Average weight costs per patient	N	Average weight costs per patient
Three complete courses of chemotherapy	73	6206.57 FF	77	5208.54 FF
Chemotherapy with side-effect and survival	11	610.76 FF	15	836.13 FF
Chemotherapy with side-effect and death	6	407.54 FF	8	788.50 FF
Early interruption of chemotherapy	10	308.50 FF	9	360.52 FF
Total average costs per patient and per branch		7533.37 FF (+ 4.6%)		7203.39 FF

Branch B: mitomycin, navelbine, cisplatin (MNP). Branch A: mitomycin, vindesin, cisplatin (MVP). N, number of patients.

Table 5
Average cost-effectiveness ratio

Average costs	Effectiveness (response rate)
Branch B = 7533.37 FF	0.25
Branch A = 7203.39 FF	0.18

Average cost effectiveness ratio:

$$\frac{7533.37}{0.25} - \frac{7203.39}{0.17} = 30\,133.48 - 42\,372.88 = -12\,239.40 \text{ FF/responder}$$

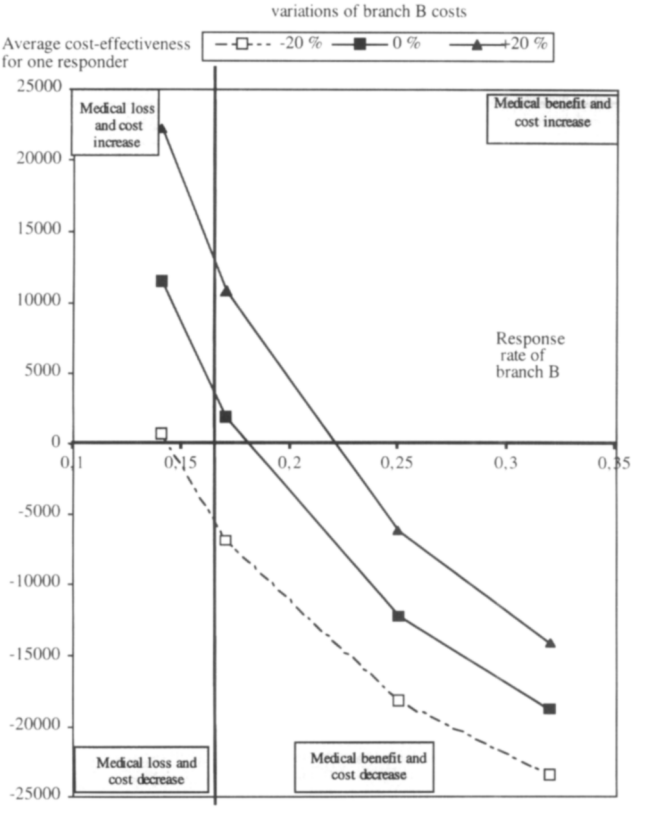


Fig. 2. Sensitivity analysis of average cost-effectiveness ratio as a function of the cost of strategy B (−20%, 0% and +20%) and the response rate of strategy B (0.15–0.45), at constant values of these parameters for strategy of branch A. The figure comprises four quadrants separated by equal response rate (vertical line) and equal cost (horizontal line). The indications on medical and cost outcomes are given in the same order as the calculation of cost-effectiveness per patient, i.e. by comparing branch B with branch A. The lower right quadrant corresponds to a greater effectiveness and less cost for branch B. The fact that this quadrant included most of the points supports the results shown in Table 5. For an effectiveness of 0.25, there was no change in the outcome (same quadrant) for a variation of 20% in costs.

survey of the patient). For branch C1, the cost was obtained by multiplying the number of injections for out-patients and in-patients (with corresponding consumptions) by the dose of the cytostatic agents. The same calculation was carried out for branch C4, where the doses and number of injections were clearly lower for the patients who dropped out. For branches C2 and C3, the calculation included the same costs as those described above together with the costs of side-effects (survivors and non-survivors).

Table 4 shows the results of average costs per branch. We found a small increase for the branch with navelbine: 7533.37 FF for branch B vs. 7203.39 FF for branch A (+4.6%).

3.3. Cost-effectiveness

A cost-effectiveness study is required for a complete economic analysis [18,19]. The cost and effects of two strategies can be compared from an average cost-effectiveness ratio. This produces a difference in cost between the two strategies for one unit of effectiveness (in the present case, a responder). The numerator is the

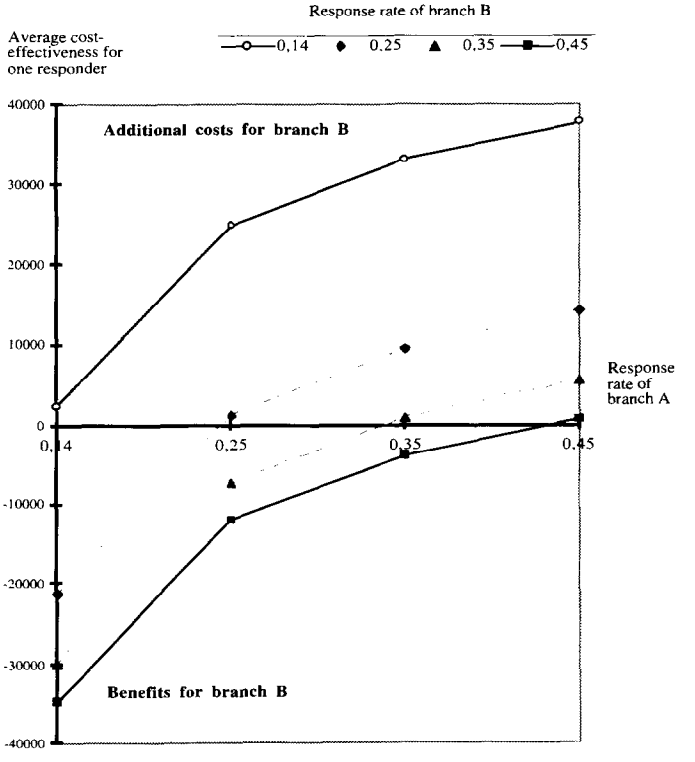


Fig. 3. Sensitivity analysis of average cost-effectiveness ratio for percentages of responders in branches B and A at constant cost. The response rate of branch A is on the abscissa, and that of branch B on the 4 plots corresponding to the values given on the straight lines (0.14–0.45). The difference in cost per responder is shown on the ordinate. Apart from a response rate of 14% for branch B, varying degrees of benefit emerged consistently for strategy B.

average cost of the two strategies and the denominator the criterion of effectiveness [19]. The results shown in Table 5 indicate that the average cost-effectiveness ratio of branch B with respect to branch A for one responder produced a benefit of 12 339.40 FF in favor of strategy B.

3.4. Sensitivity

We carried out two types of sensitivity analysis as not all parameters could be varied at once. Firstly, an analysis of the sensitivity of strategy B on cost and response rates (the aim of the study). Fig. 2 shows that there are 4 possible results for the difference in average cost-effectiveness. By varying the cost by 20% around the observed value, most of the points were found to lie in the quadrant of medical benefit and decrease in cost, which is indicative of the validity of the observed results. A benefit for strategy A using the values obtained in the present study was only produced by a considerable increase in branch B costs with an effectiveness below 0.20. Secondly, an analysis of the sensitivity on response rates of the two strategies assuming constant costs (Fig. 3). The plots show the differences in average cost-effectiveness ratios with the excess costs of branch B (upper part of Fig. 3) and the benefits of branch B (lower part of Fig. 3) as a function of response rate.

4. Discussion

Cost-analysis of the hospital administration of two chemotherapeutic regimens showed that the combination MNP had a low increase of average direct costs per patient. However, if we realized a cost-effectiveness analysis, MNP had the more favourable ratio.

4.1. Methodological issues

(a) These results were obtained from a randomized trial and are only valid for this particular group of patients, although the statistically comparable nature of the two groups suggests that the results could be extrapolated to other groups of patients with non-surgical lung cancer.

(b) The direct costs were recorded from the hospital perspective. The decision to analyze the cost of the two chemotherapeutic regimens was justified by the fact that they made up a significant proportion of the total expenditure (around 2/3). In French hospital accounting, three categories of expenditure are distinguished: staff expenditure, medical expenditure (consumables and pharmaceutical drugs), logistic expenditure (including the cost of laundry, catering, heating, etc.). We did not analyse the last category since the study was randomized on a per center and per strategy basis and the hospital infrastructure costs tended to cancel out. So we only included the cost of drugs and their side-effects (in terms of time spent, diagnosis procedures and treatment). It would, however, be worthwhile to consider transportation costs from the viewpoint of the paying agency (the Social Security System) as the higher number of navelbine injections entails more journeys to the hospital and hence a higher transportation cost, but it was not the objective of the study.

We did not take account of indirect costs such as those due to days of work lost

by the patients, and intangible costs stemming from the repercussion of the disease on the patient's lives.

(c) Economic studies, in lung cancer, induce methodological difficulties. Side-effects are responsible for either early deaths (with low costs), or long hospital stays (with high costs). Transfer of a few patients from one category to another can change the calculation of total costs. We chose to calculate average costs according to the type and outcome of the side-effect in an attempt to minimize bias.

The second group of difficulties is in relation to the multicenter study. As in another study [10], we recorded the volumes consumed per patient in each center and the costs were derived from the data obtained from two centers. This highlights the limitations of this type of study, which does not produce exact calculations. The cost analysis could certainly be improved in France by application of analytical accounting procedures.

4.2. Economic studies of lung cancer

Such studies are required in view of the high incidence of lung cancer [9], and we have attempted here to show that economic factors can be included in a randomized trial given the limitations mentioned above. The results obtained were regarded as complementary to those of the clinical protocol. In a similar study, Jaakkimainen et al. [10] showed that, relative to best supportive care, the combination of cyclophosphamide, adriamycin and cisplatin led to an increased survival along with a reduction in hospital costs. On the other hand, the combination of cisplatin and vindesine led to an increased survival along with an increased cost relative to supportive treatment. Thus it can be seen that different regimens may have different economic consequences. In another study, Richardson et al. [16] showed that application of a diagnostic algorithm for assessment of the extension of small cell cancers could save a third of the initial investigatory costs.

In France, Quantin et al. [13] have evaluated the hospital costs of non-metastatic lung cancers. They showed the importance of chemotherapy in such costs, and the need to take them into account in economic analyses.

4.3. Choice of strategy

In the hypothesis of equivalence between the two treatments, the methodology to use is the cost-minimization. It needs comparison between average costs. The results show a small difference (4.6%) in favor of strategy A (MVP). This difference may have been due to chance.

In the hypothesis of effectiveness difference, if we consider that there is a lack of strength of clinical study, the methods are based on cost-effectiveness analysis. We found a benefit for the branch B (MNP).

The medico-economic choice is thus in favor of branch B. This remained the case over a certain range of costs and response rates in strategy B as indicated by the sensitivity analysis. This will need to be supported by complementary analyses of cost over a longer period such as those required for a QALY study (symptom or relapse-free periods, or survival).

Nevertheless, economic conclusions should not be viewed in isolation as they

reflect concerns that differ from therapeutic and diagnostic considerations [6]. They need to be viewed along with the findings of studies evaluating outcome (survival rates) or impact on the patient (quality of life).

In conclusion, we showed that a clinical trial can usefully include an analysis of economic factors. Consideration of the results in terms of effectiveness may contrast with those based on pure cost. It should be borne in mind that the results of an accounting analysis of a therapeutic strategy are an oversimplification, and that the economic choice is derived by evaluating the cost of two strategies with respect to their effectiveness. The decision is ultimately a medical one, which needs to weigh up the advantages and disadvantages of a particular regimen or protocol. The economic criteria described here thus form part of the overall decision process, which should include other criteria including those evaluating quality of life. Future clinical trials may stand to benefit from more systematic use of economic analytical procedures.

Acknowledgements

We thank A. Lafuma, MD, for his technical assistance in the economic evaluation and for his critical review of the manuscript.

Appendix 1

Example of calculation of cost of side-effects
Health care expenditure

Number of days in hospital for treatment of side-effects
Daily time spent by hospital physician (gross 1993 salary)
Daily time spent by internist or medical student (gross 1993 salary)
Daily time spent by nurse (gross 1993 salary)
Daily time spent by nursing auxiliary (gross 1993 salary)

Investigations for diagnosis of side-effects

Costs are calculated from scales established by the French Social Security System

Treatment of side-effects

Nature of drug used
Average price per unit (not including sales tax) from the pharmacy departments of the Limoges University Hospital and the Public Hospitals in Lyon
Dosage of pharmaceutical products
Number of days.

Example of calculation for a given side-effect

Hematological side-effect requiring 3 days hospital treatment (average nursing time per day = 90 min, average nursing auxiliary time = 40 min, average hospital physician's time = 20 min, mean internist's time = 30 min), laboratory investigations on admission, additional blood counts (2 pellets), course of antibiotics (augmentin* — oflocet*):

Nursing cost	90 × 1.89 × 3	510.30 FF

Auxiliary nursing cost	40 × 1.33 × 3	159.60 FF
Hospital physician cost	20 × 4.35 × 3	130.50 FF
Internist cost	30 × 1.23 × 3	73.80 FF
Laboratory tests		484.00 FF
Blood counts		70.40 FF
2 pellets		860.00 FF
Augmentin*		167.40 FF
Oflocet*		263.52 FF
Total		2867.32 FF

The side-effects were added together for each arm, type and outcome.
The totals were listed under the various categories, we calculated an average cost according to the side-effect and the outcome (Table 1).

Appendix 2

Example of calculation of cost for the branches of the tree

Branch C1 3 complete courses of regimen B (MNP)

206 injections of cisplatin-mitomycin-navelbine as an in-patient and 847 injections of navelbine as an out-patient for 73 patients corresponding to 38 505 mg of cisplatin, 3110 mg of mitomycin, 32 940 mg of navelbine. Costs of materials and nursing time are listed in Tables 2 and 3.

(206 × 245.18 FF) + (38 505 mg × 1.38 FF) + (3110 mg × 7.83 FF) + (847 × 104.31 FF) + (32 940 mg × 12.30 FF) = 621 508.96 FF. This value is divided by the number of patients in this branch (n = 77): 621 508.96/77 = 8513.22 FF per patient.

Branch C2 Occurrence of side-effects with survival of patient in arm B (navelbine): 11 cases. 16 injections of combination as in-patient, 54 injections of navelbine as out-patient, 2731.4 mg of cisplatin injected, 189.16 mg of mitomycin, 1735.47 mg of navelbine.

(16 × 245.18 FF) + (2731.4 mg × 1.38 FF) + (189.16 mg × 7.83 FF) + (54 × 104.31 FF) + (1735.47 mg × 12.30 FF) = 36 153.02 FF.

Cost of side-effects = 28 441.96 FF (derived from Table 1)

The cost with respect to branch C2 = 36 153.02 FF + 28 441.96 FF = 64 594.98 FF. This value is divided by the number of patients (n = 11) = 5872.27 FF.

References

[1] Bonomi Ph. Platinum/etoposide therapy in non-small cell lung cancer. Oncology 1992; 49: 43–50.
[2] Cellerino R, Tumarrello D, Guidi F, et al. A randomized trial of alternating chemotherapy versus best supportive care in non-small cell lung cancer. J Clin Oncol 1991; 9: 1453–1461.
[3] Chauvin F, Lasset C, Trillet-Lenoir V, Souquet PJ. Evaluation clinique et économique du bilan initial des cancers du poumon à petites cellules in Sofestec ed. Les outils de l'évaluation économique en cancérologie, aspects méthodologiques. Paris: Institut Gustave Roussy, 1992; 19–30.
[4] Collin C, Delahaye F, Ecochard R, Landrivon G, Rabilloud M, Teboul F, Matillon Y. L'analyse de la décision médicale. Arch Mal Coeur 1993; 86: 1597–1603.
[5] Depierre A, Lemarie E, Dabouis G, Garnier G, Jacoulet P, Dalphin JC. A phase II study of

Navelbine (Vinorelbine) in the treatment of non-small cell lung cancer. Am J Clin Oncol 1991; 14: 115–119.

[6] Detsky AS, Naglie IG. A clinician's guide to cost-effectiveness analysis. Ann Int Med 1990; 113: 147–154.

[7] Dillman RO, Seagren SL, Propert KJ, et al. A randomized trial of induction chemotherapy plus high-dose radiation versus radiation alone in stage III non-small cell lung cancer. N Engl J Med 1990; 323: 940–945.

[8] Drummond MF, Stoddart GL, Torrance GW. Methods for economic evaluation of health care programmes, 3rd ed. London: Oxford University Press, 1990; 182.

[9] Evans WK. Rationale for the treatment of non-small cell lung cancer. Lung Cancer 1993; 9: 5–14.

[10] Jaakkimainen L, Goodwin PJ, Pater J, Warde P, Murray N, Rapp E. Counting the costs of chemotherapy in a national cancer institute of Canada randomized trial in non-small cell lung cancer. J Clin Oncol 1990; 8: 1301–1309.

[11] Le Chevalier T, Pujol JL, Douillard JY, et al. A European multicenter randomized study comparing navelbine alone vs navelbine cisplatin vs vindesine cisplatin in 612 patients with advanced non-small cell lung cancer (NSCLC). Proc Am Soc Clin Oncol 1992; 11: 289.

[12] Perol M, Guerin JC, Kleisbauer JP, et al. Multicenter randomized trial comparing cisplatin mitomycin vindesine versus cisplatin mitomycin navelbine in non-small cell lung cancer (NSCLC). Lung Cancer 1994; 11; S1–85.

[13] Quantin C, Zehal S, Dusserre L, Simon I, Foucher P, Michiels D, Durnet MJ. Evaluation du coût des cancers bronchiques primitifs. Inform Santé, 1994; 17: 45–49.

[14] Quoix E, Dietemann A, Charbouneau J, et al. La chimiothérapie comportant du cisplatin, est-elle utile dans le cancer bronchique non-microcellulaire au stage IV? Résultats d'une étude randomisée. Bull Cancer 1991; 78: 341–346.

[15] Rapp E, Pater JL, Willau A, et al. Chemotherapy can prolong survival in patients with advanced non-small cell lung cancer; report of a Canadian multicenter trial. J Clin Oncol 1988; 6: 633–641.

[16] Richardson GE, Venzon DJ, Phelps R, Edison M, Brown M, Frame JN, Ihde DC, Johnson BE. Application of an algorithm for staging small-cell lung cancer can save one third of the initial evaluation costs. Arch Intern Med 1993; 153: 329–337.

[17] Teboul F, Moatti JP, Colin C. L'analyse économique des stratégies médicales: du conflit à la complémentarité avec la clinique. J Econ Méd 1991; 9: 85–96.

[18] Urban T, Lebeau B. Chimiothérapie des cancers bronchiques non à petites cellules stage III. Oncologica 1994; 8: 33–39.

[19] Weiden PL, Piantadosi S. Preoperative chemotherapy (cisplatin and fluorouracil) and radiation therapy in stage III non-small cell lung cancer a phase II study of the Lung Cancer Study Group. J Natl Cancer Inst 1991; 83: 266–273.

[20] Woods RL, Williams DJ, Levi J, et al. A randomized trial of cisplatin and vindesine versus supportive care only in advanced non-small cell lung cancer. Br J Cancer 1990; 61: 608–611.