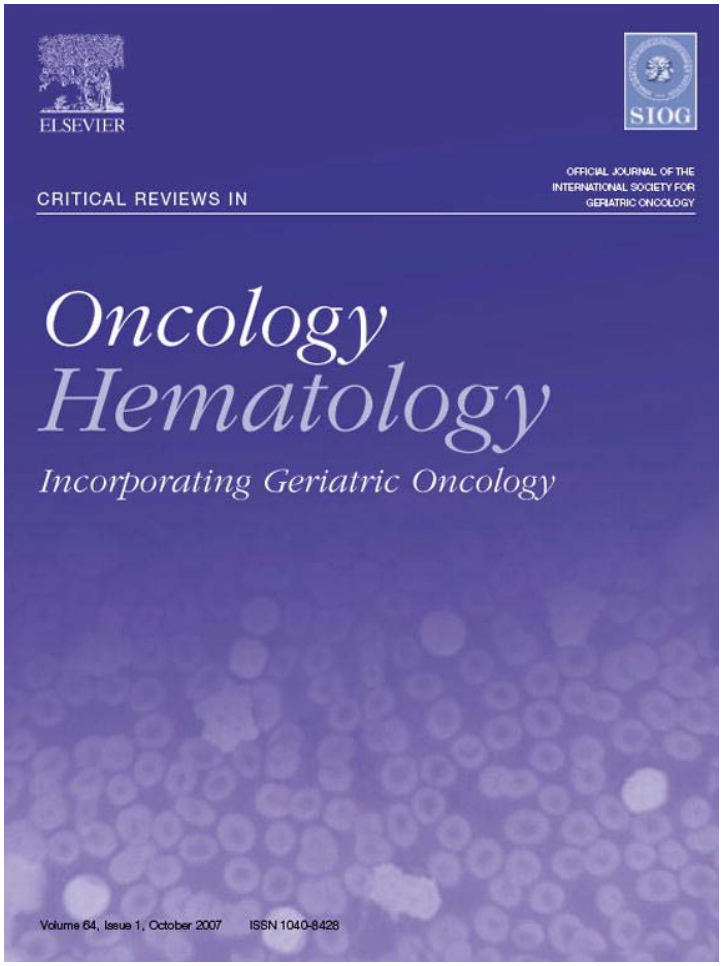

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An open multicenter phase II trial of docetaxel–gemcitabine in Charlson score and performance status (PS) selected elderly patients with stage IIIB pleura/IV non-small-cell lung cancer (NSCLC): The GFPC 02-02a study☆

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Contents

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Abstract

The aim of this study was to determine the impact of patient selection based on age, comorbidity and performance status on the efficacy of platinum-free combination therapy on non-small-cell lung cancer after 65 years of age.

We analyzed the overall response rate, the median survival time, the 1-year survival rate, toxicity and quality of life after one to three 6-week cycles of docetaxel 30 mg/m^2 weekly and gemcitabine 900 mg/m^2 at weeks 1, 2, 4 and 5. Fifty patients (median age 73.7 years) were eligible. The mean number of comorbid conditions per patient was 0.8 [Balducci L. Lung cancer and aging. ASCO 2005. Educational book. p. 587–91; Piquet J, Blanchon F, Grivaux M, et al. Primary bronchial carcinoma in elderly subjects in France. Rev Mal Respir 2003;20:691–9; Jatoi A, Hillman S, Stella P, et al. Should elderly non-small-cell lung cancer patients be offered elderly-specific trials? Results of a pooled analysis from the North Central Cancer Treatment Group. J Clin Oncol 2005;23:9113–9; Balducci L, Extermann M. Management of cancer in the older person: a practical approach. Oncologist 2000;5:224–37]. Forty-five patients were assessable: 17 (34%) had an objective response, 18 (36%) had stable disease and 10 progressed (20%). The median survival time was 7 months and the 1-year survival rate 23.5%. The main grade III–IV adverse event was neutropenia (32% of patients).

Conclusion: Platinum-free dual-agent chemotherapy gives similar results in patients over 65, selected on the basis of their precise age and comorbidity, to that reported in younger subjects.

Keywords: Chemotherapy; Comorbidity; Elderly; Lung cancer; Phase II trial

1. Introduction

Although two-thirds of patients with non-small-cell lung cancer (NSCLC) are over 65 years of age [1,2], clinical trials specifically involving elderly patients are rare in the field of thoracic oncology. Yet the value of such studies has now been demonstrated [3], and the notion of "clinical benefit" is now gradually supplanting classical quantitative outcome measures – the tumor response rate and the survival rate – in the geriatric setting [4].

In patients under 65, who are in good general health [7], the recommended first-line treatment for metastatic or locally advanced NSCLC consists of dual-agent chemotherapy based on a platinum salt. There is no consensus on the definition of "elderly" patients. The cutoff is frequently 65 years in North American studies, but 70 or even 75 years in Europe [5]. Cisplatin is highly toxic in elderly subjects, and the likely risk–benefit ratio of this treatment must be carefully assessed before treatment [5]. Studies specifically devoted to elderly patients have shown an advantage in terms of survival and quality of life with single-agent (vinorelbine) chemotherapy relative to best supportive care [6]; they have also shown the feasibility of dual-agent chemotherapy without platinum, but the superiority of such regimens over single-agent therapies has not been formally demonstrated [7–9]. In contrast, two-drug regimens based on a platinum salt have given rather disappointing results [10].

A recent phase II study published by Neubauer et al. [11] showed that it is possible to use a combination of docetaxel and gemcitabine administered weekly for 6 weeks during 8-week cycles offers a response rate better than 20% and acceptable adverse effects, including hematologic toxicity.

One limitation of these studies is that the authors selected patients over 65 years of age, like younger patients, solely on the basis of their performance status. Yet performance status alone is probably not a very discriminatory stratification tool in this age range. Indeed, the patient's precise age and comorbid disorders may influence the response to chemotherapy, or at least its tolerability [12]. The Charlson score (Appendix A) is an elderly-specific stratification tool combining age and comorbidity [13]. A score above 2 has vital prognostic value [14], independently of performance status [15].

On this basis, NSCLC patients over 65 years can be divided into at least four subpopulations: (1) patients under 70, or perhaps under 75, who are in excellent general health and can probably be treated in the same way as younger patients (platinum-based dual-agent chemotherapy); (2) patients under 70 who are in mediocre general health and patients over 70 years who have comorbidity but are in good general health, who can receive dual-agent chemotherapy without platinum; (3) patients under 70 with comorbidity and those over 70 who are in poor general health (fragile elderly subjects) who can probably only tolerate monotherapy; and finally (4) as at younger ages, some elderly patients who are in very poor general health or who have severe comorbidity and who should not be treated.

The aim of this study was to determine the impact of patient selection based on age, comorbidity and performance status on the efficacy of platinum-free combination therapy on non-small-cell lung cancer after 65 years of age with docetaxel and gemcitabine [11–16].

2. Patients and methods

2.1. Study design

This was a multicentre, open-label, phase 2 study (code GFPC 02-02a) of docetaxel plus gemcitabine in selected elderly patients with advanced NSCLC. The pri-

mary objective was to evaluate the ORR (complete responses [CR] + partial responses [PR]) using the Response Evaluation Criteria in Solid Tumors (RECIST) [17]. Secondary objectives were to assess the disease control rates (CR + PR + stable disease [SD]) at study closure, also using RECIST, as well as progression-free survival (PFS) and overall survival (OS). We also evaluated the safety and tolerability of the dual combination in this population. Quality of life was evaluated using the Spitzer index [18] and the Lung Cancer Symptom Scale (LCSS) [19]. The study protocol was approved for all sites by an independent ethics committee in Marseille, and the study was conducted in accordance with Good Clinical Practices and the Declaration of Helsinki (World Medical Association 1997).

Table 1
Geriatric inclusion criteria

Age score	Charlson score	Age + Charlson score	PS	Regimen
	0–2	[2–4]	0–1	Ineligible
	0–2	[2–4]	2	D + G
65–69 = 2	3–4	[5–6]	0–1	D + G
	3–4	[5–6]	2	Ineligible
	5–6	[7–8]	0–2	Ineligible
	0–1	[3–4]	0–1	D + G
70–79 = 3	0–1	[3–4]	2	Ineligible
	2–5	[5–8]	0–2	Ineligible
	0	[4]	0–1	D + G
80–89 = 4	1–4	[5–8]	0–1	Ineligible
	Any	Any	2	Ineligible

2.2. Patients

The oncologic inclusion criteria were as follows: cytologically or histologically proven NSCLC of pleural stage IV or IIIB, not previously treated with chemotherapy, with a measurable tumor (RECIST criterion 18); life expectancy more than 3 months and biological results compatible with chemotherapy (bilirubin <1.25 ULN, transaminase activity <3 ULN, alkaline phosphatase <2.5 ULN, polymorphonuclear neutrophil count >1.5 G/l and platelet count >100 G/l).

The geriatric inclusion criteria comprised age, the Charlson comorbidity score and performance status (Table 1); this excluded patients aged from 65 to 69 years with mild comorbidity and a PS of 0 or 1 (who were eligible for more aggressive treatment) and patients whose comorbidity and/or PS were too severe.

The non-inclusion criteria were mainly histological (small-cell lung cancer, bronchioloalveolar carcinoma). The following patients were not eligible for the study: patients previously treated with chemotherapy, patients with only bone metastasis, pleuresy or carcinomatous lymphangitis (impossible to measure the response); patients with symptomatic brain metastases, unstable heart disease, uncontrolled infection, grade ≥2 neuropathy; another concurrent metastatic cancer or permanent contraindications to the use of steroids.

The geriatric non-inclusion criteria were age > 89 years and a combined comorbidity–PS score incompatible with the values shown in Table 1.

2.3. Treatment

The treatment schedule (see Fig. 1) comprised one to three 8-week cycles of a combination of docetaxel 30 mg/m^2 weekly for 6 weeks and gemcitabine 900 mg/m^2 administered at weeks 1, 2, 4 and 5. The response was assessed after each cycle, with a final assessment between D157 and D163. Erythropoietin (epoietin alpha, 400,000 units once a week) was administered whenever the hemoglobin level fell below 12 g/dl. The use of growth factors was left to the individual investigator. Before the beginning of each infusion,

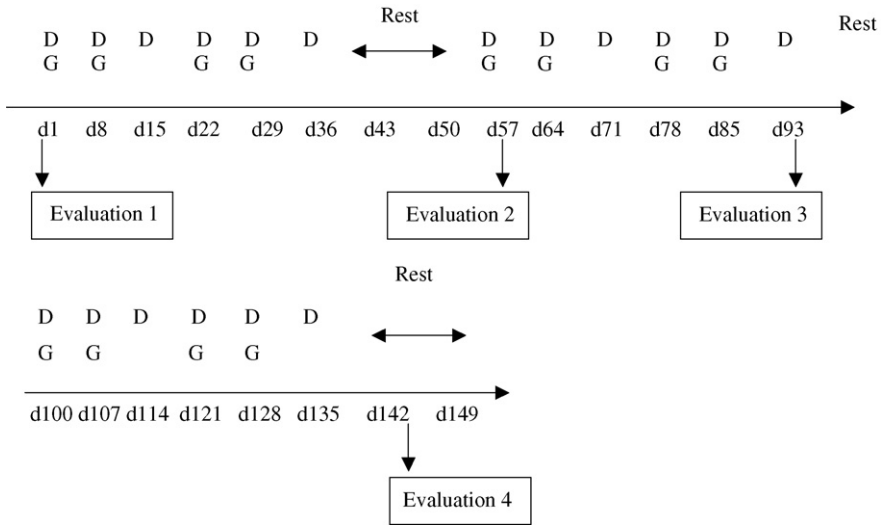

Fig. 1. GFPC 02–02 study flowchart: (D) docetaxel, (G) gemcitabine, (d) day.

the patients were reassessed to ensure that their neutrophil count was at least 1.5×10^9/l and their platelet count at least 100×10^9/l. Chemotherapy infusions could be postponed for up to 2 weeks if the patient had not fully recovered from the toxicity of the previous infusion. If chemotherapy needed to be delayed twice (whether in consecutively cycles or not), or if severe toxicity occurred (as defined in the protocol), the doses of docetaxel and gemcitabine were reduced by 25%; if toxicity persisted, a second dose reduction of 50% was allowed. No dose re-escalation was allowed. The dose intensity (dose received/expected dose) was calculated for each drug and each cycle. Chemotherapy was stopped permanently after two dose reductions if toxicity was judged unacceptable or reached the level defined in the protocol; in case of documented disease progression; once the planned treatment had been completed; if the patient refused to continue in the trial.

2.4. Assessments

2.4.1. Efficacy

Efficacy was based on the response rate, as often in phase II studies. The predicted response rate served to calculate the required sample size.

The tumor response was assessed objectively with the RECIST method at the end of each treatment cycle. All objective responses were confirmed 4 weeks later. Patients were considered to have controlled disease if they had an objective response lasting ≥4 weeks or stable disease lasting ≥6 weeks during the study or at study closure.

Secondary endpoints were progression-free survival (PFS), assessed from the date of first treatment to the earliest date of disease progression, or death of any cause, or the last on-trial tumor assessment and overall survival (OS), assessed from the date of first treatment to the date of death of any cause or the last date the subject was known to be alive. All responses were reviewed and confirmed by an expert panel convened by GFPC (Groupe Français de PneumoCancérologie).

2.4.2. Safety and tolerability

Patients were monitored for adverse events, laboratory and vital sign abnormalities and electrocardiographic changes, throughout the study and for 30 days following the last dose of study treatment. The nature, incidence and severity of adverse events were recorded and graded with the NCI-CTC system version 2.0 (National Cancer Institute, 1999).

2.5. Statistical analysis

Quantitative data were expressed as the number, mean, standard deviation and range; qualitative data were expressed as the number and frequency. All tests were two-sided, and significance was assumed at $p > 0.05$. Quantitative variables were compared with Student's t test or with Wilcoxon's test when the groups were too small or the data were not normally distributed. Qualitative parameters were compared with the Chi^2 test for theoretical group sizes above 5, and with Fisher's test in other cases.

Assuming that the study treatment should be rejected if the objective response rate was 15% or less, and would be validated by a response rate of 30% or more, with an alpha risk of 0.07 and a beta risk of 0.08, the number of subjects to be included in the first phase was 16 and the total number of patients to be included was 45 [20].

The intent-to-treat (ITT) population (i.e. all patients who were enrolled and received at least one dose of study medication) served to analyze efficacy. The proportions of patients who had an objective tumor response and stable disease were summed together with the 95% confidence interval (CI) to define the controlled disease. PFS and OS were assessed by means of Kaplan–Meier analysis at study closure. A Cox model was used to identify explanatory variables for survival among the following: sex, age, the comorbidity score, performance status, the Spitzer score at enrollment and the disease stage.

Tolerability and quality-of-life endpoints were described by using standard summary statistics for all treated patients.

The analysis of quality of life, done during the initial work-up (intention-to-treat) and at the end of each cycle, used the Spitzer index [18] and the Lung Cancer Symptom Scale (LCSS) [19]. Each item of the Spitzer score was attributed a score of 0–2, with higher values reflecting better health. A mean global score is then calculated. Each item of the LCSS questionnaire is scored from 0 to 10; the higher the score, the greater the symptom intensity. The LCSS questionnaire yields two scores: a symptom score calculated from the first six items (appetite, fatigue, cough, breathlessness, hemoptysis and pain). The global score is derived from the last three items (symptom severity, discomfort during routine activities and quality of life).

Quantitative scores are expressed as the mean, the median and the confidence interval. The groups were compared with Fisher's exact test. Statistical analyses were done with SAS software version 8.02 (Institute INC, Carry, USA).

3. Results

3.1. Patients

From June 2003 to December 2004, 19 participating centers enrolled 50 patients (Table 2). The number of patients per center was two on average. Enrolments were homogeneously distributed among the participating centers. The majority of patients (89.1%) had stage IV NSCLC, consisting of epidermoid carcinoma in 38% of cases, adenocarcinoma in 38% and undifferentiated forms in 24%. Eighty-four percent of the patients were aged between 70 and 79 years, had one or more comorbid disorders and had a performance status to 0 or 1 (Table 3). The median number of cycles received was 2 + 0.6 (i.e. 16 weeks of treatment). The reasons for premature

Table 2
Characteristics of the patients

Age (years) (mean [range])	73.7 [65–82]
Sex (%)	
Male	78
Female	22
ECOG PS (%)	
0	42
1	54
2	4
Clinical stage (%)	
IV	88
IIIB	12
Histology (%)	
Squamous cell	38
Adenocarcinoma	38
Undifferentiated	24
Charlson score (mean [range])	0.8 [0–4]
Age–comorbidity score (mean [range])	3.7 [2–6]
Weight loss (%)	
>10%	23.90

Table 3
Age and comorbidity

Age score	Charlson score	Age + Charlson score	PS	Number of patients (total, $n = 50$)
65–69 = 2	0–2	[2–4]	2	2
	3–4	[5–6]	0–1	4
70–79 = 3	0–1	[3–4]	0–1	42
80–89 = 4	0	[4]	0–1	2

Table 4

Dose intensity	Cycle 1 (%)	Cycle 2 (%)	Cycle 3 (%)	Total (%)
Docetaxel	81.7	83.3	69.2	81.7 [67.1–88.9]
Gemcitabine	96.1	98.5	91.0	92.9 [74.7–99.4]

Table 5
Reasons for study withdrawal

Progression	15
Toxicity	11
Fatigue	6
Infection	2
Ungueal	1
Interstitial pneumonia	2
Intercurrent conditions	2
Ischemic colitis	1
Pulmonary embolism	1
Patient's decision	3

treatment cessation are summarized in Table 4. The per-cycle dose intensity is summarized in Table 5.

3.2. Response and survival

Six of the first 16 patients had objective responses, authorizing the study to continue into the second phase. The analysis of efficacy in the 45 assessable patients showed objective responses in 17 patients (34%: 21.6–48.7), stabilization in 18 patients (36%: 22.9–50.8) and progression in 10 patients (20%: 10–33.7). The median duration of the objective responses was 4.86 (3.53–7.6) months, the median time to progression was 4.93 (4.23–6.9) months (Fig. 2), the median survival time was 7.07 (5.63–8.83) months and the 1-year survival rate was 23.5% (Fig. 3).

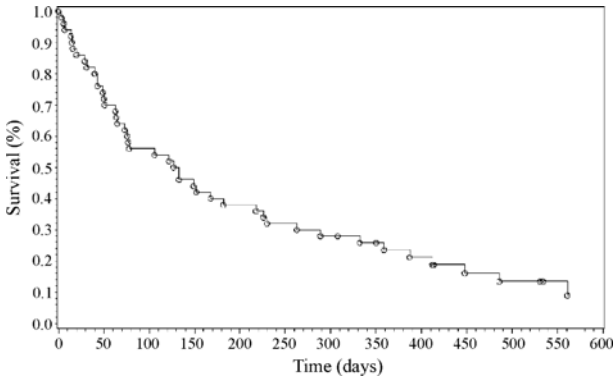

Fig. 2. Kaplan–Meier curve for time to progression ($n = 50$).

3.3. Quality of life

Before treatment, quality of life was analyzed in 44 patients who completed the initial assessment; the global median LCSS score was 3.16 (95% CI 0.07–8.00) the mean symptom score was 2.16 (95% CI 0.08–5.28) and the mean Spitzer score was 7.5 (95% CI 3–10). Fig. 4 shows changes in the LCSS score over time, and Fig. 5 according to the treatment response. The score increased among patients who progressed, although the difference was not significant because of the small number of patients concerned. These scores did not change significantly over time (Fig. 4), even when the analysis took the treatment response into account (Fig. 5).

Univariate analysis showed that survival was influenced by gender ($p < 0.019$ in favor of women), the disease stage ($p = 0.016$) and the Spitzer score ($p < 0.0001$). The results of

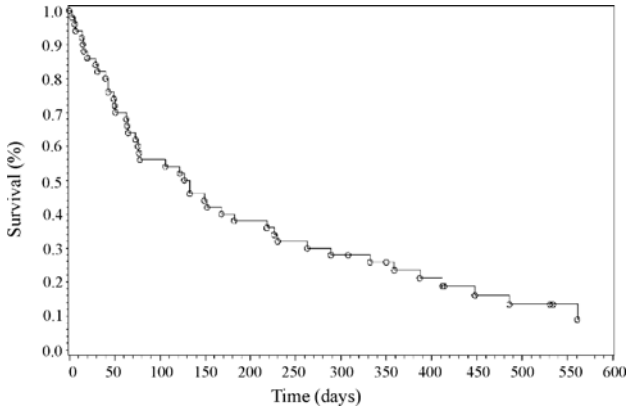

Fig. 3. Global survival (Kaplan–Meier) ($n = 50$).

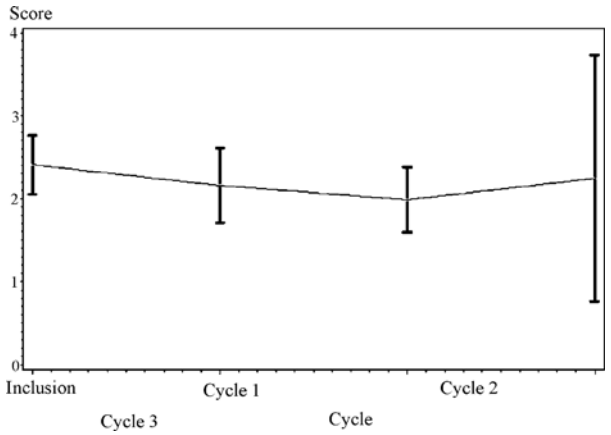

Fig. 4. Global LCSS score. Changes over time ($n = 44$), LCSS: Lung Cancer Symptom Scale.

the multivariate Cox model must be interpreted with care, given the small group sizes. Two variables remained significantly associated with survival: the disease score and the Spitzer score. The relative risk was (HR = 6.15, $p = 0.016$) for stage IV versus stage III B, and (HR = 1.55, $p < 0.0001$) for a one-point increase in the Spitzer score relative to baseline.

3.4. Safety

The ITT population of 50 patients was assessable for safety. The most common non-hematological adverse events were fatigue, diarrhea, nausea, constipation, hair loss and peripheral neuropathy (Table 6). The most common hematological adverse events were neutropenia and anemia, although the latter was mainly grade 1 or 2 (Table 5); Epoietin alpha was administered to 58% of patients; 18% of patients received red cell transfusions (12% during the first cycle) and 1.3% received platelets. Two patients died with interstitial pneumonia, one of clinical progression. Only one death

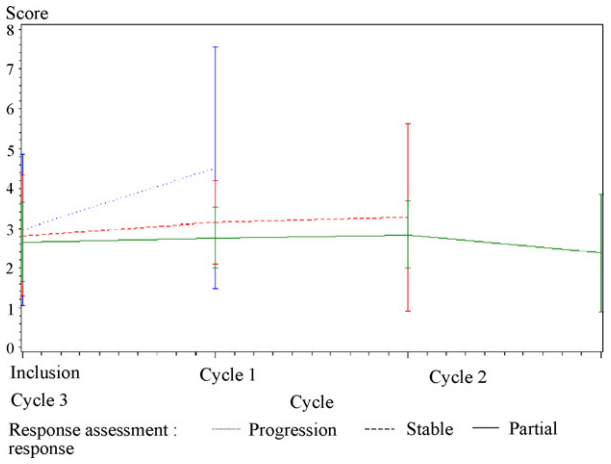

Fig. 5. LCSS symptom score. Study of changes over time in responders ($n = 17$), patients with stable disease ($n = 18$) and patients with progressive disease ($n = 10$).

Table 6
Most common adverse events

Adverse event	Docetaxel + gemcitabine	
	Grade 1/2 ($n = 50$)	Grade 3/4 ($n = 50$)
Anemia	29 (58%)	6 (12%)
Neutropenia	27 (54%)	6 (12%)
Thrombocytopenia	25 (50%)	4 (8%)
Nausea/vomiting	17 (34%)	2 (4%)
Fatigue	20 (40%)	15 (30%)
Peripheral neuropathy	10 (25%)	1 (2%)
Diarrhea	15 (30%)	2 (4%)
Alopecia	4 (8%)	5 (10%)
Infection	4 (8%)	4 (8%)

was attributed to the docetaxel–gemcitabine combination, in keeping with previous studies [21,22].

4. Discussion

This phase II trial shows that patient selection based on age, performance status and comorbidity (Charlson score) allows more appropriate treatment of elderly subjects with NSCLC. The docetaxel–gemcitabine combination gave a response rate of 34%.

The disease was controlled in 70% of patients, and the 1-year survival rate was 23.5%. Toxicity, including hematologic toxicity, was limited; 32% of patients had grade 3/4 neutropenia, and only 18% needed transfusions, confirming the value of erythropoietin in this setting [23]. These results demonstrate the feasibility of this approach to patient selection, permitting dual-agent therapy in NSCLC patients over 70 years who are in good general condition. These results therefore demonstrate the feasibility of this dual-agent chemotherapy in these patients, most of whom were aged between 70 and 79 years but were in good general health and/or had little comorbidity.

These results are consistent with recently published data [10] suggesting that this combination is as effective as and less toxic than platinum-based two-drug regimens. Thus, in the elderly, the carboplatin–vinorelbin combination [10] controls the disease in 45% of patients with a median survival time of 7.8 months, but grade 3/4 neutropenia occurs in 68% of cases; similarly, the combination of carboplatin-AUC5 and paclitaxel 175 mg/m^2 [24] controls the disease in 57.5% of cases with a median survival time of 7.8 months, but grade 3/4 neutropenia occurs in 37.5% of cases.

This dual-agent chemotherapy also appears to be more active than navelbine or gemcitabine monotherapy [25]. It appears to be equivalent to consecutive treatment with vinorelbine then gemcitabine, which gives objective responses in 38% of patients, a median survival time of 8 months and a 1-year survival rate of 28.5% [26]; or the gemcitabine–vindesine combination, which gives objective responses in 38.6% of patients [27].

This platinum-free schedule is based on a phase III randomized study in younger patients [28–30]. In elderly

patients, weekly administration has been reported to be poorly effective [7–9], while other publications (of phase II trials) show that this schedule is associated with less toxicity (32% of grade IV neutropenia) [9–11,16,31].

In our study, two patients died with toxicity-related interstitial pneumonia. One of these patients had disease progression suggestive of carcinomatous lymphangitis. Only one death was attributed to the docetaxel–gemcitabine combination, a rate (2%) in keeping with the literature: one death among 81 patients in Quoix's study [25], two deaths among 36 patients in Chen's study [21] and one death among 42 patients in Bhatia's study [32]. The number of deaths appears acceptable.

The main originality of this study is that the patients were selected on the basis of geriatric criteria combining the precise age, performance status and comorbidity, expressed using the Charlson score. These three items stratify the elderly population more precisely and make different studies of patients over 65 more comparable. It is noteworthy that a recent study clearly showed that performance status does not correlate with the Charlson score [33].

Although this classification improves patient selection and allows treatment to be individually tailored, it probably remains suboptimal. Indeed, the Charlson score fails to give sufficient weight to certain comorbidities, such as moderate to severe renal failure, which is frequent in this population [34]. Above all, it does not take into account other factors of vulnerability, such as depression and cognitive disorders [35]. Balducci et al. [1] have shown the importance of specific geriatric assessment taking into account functional, mental, social and nutritional status and daily activities.

If one were to follow SIOG recommendations [36], it would be necessary to use a minimum of a geriatric depression scale, the Folstein Mini Mental Status score and a test of performance status, such as the Get Up and Go test, ADL and especially IADL, which, in the MILES trial [16], was an independent prognostic factor. Thus, a recent study [37] showed that quality of life and instrumental activity index of daily living could be a good prognostic factor when combined with the Charlson score and performance status.

The main advantage of these tests is that they improve patient selection and facilitate comparisons between different studies.

However, a balance must be found between a highly detailed geriatric evaluation, which is not compatible with routine practise, and preliminary use of a simplified geriatric index gériatrique, followed if necessary by a more detailed assessment than that recommended by an expert panel in 2004 [10].

5. Conclusion

In elderly patients with NSCLC, selection based on age, general condition and comorbidity can identify those likely to benefit from dual-agent chemotherapy. Our results show that such selection is feasible and that weekly dual-agent therapy has satisfactory efficacy and acceptable toxicity. This phase II trial is a first step towards more discriminant selection of elderly patients. We are now planning a phase III trial to validate a simplified geriatric index for assigning elderly NSCLC patients to either single-agent or dual-agent therapy.

Reviewers

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Appendix A

Comorbidity	Points
Myocardial infarct	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes	1
Diabetes with end organ damage	2
Hemiplegia	2
Moderate or severe renal disease	2
Any tumor	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
AIDS	6
Total	

Age	Score
50–59	1
60–69	2
70–79	3
80–89	4
90–99	5

References

[1] Balducci L. Lung cancer and aging. ASCO 2005. Educational book. p. 587–91.

[2] Piquet J, Blanchon F, Grivaux M, et al. Primary bronchial carcinoma in elderly subjects in France. Rev Mal Respir 2003;20: 691–9.

[3] Jatoi A, Hillman S, Stella P, et al. Should elderly non-small-cell lung cancer patients be offered elderly-specific trials? Results of a pooled analysis from the North Central Cancer Treatment Group. J Clin Oncol 2005;23:9113–9.

[4] Balducci L, Extermann M. Management of cancer in the older person: a practical approach. Oncologist 2000;5:224–37.

[5] Rossi A, Gridelli C. Chemotherapy of advanced non-small-cell lung cancer in elderly patients. Ann Oncol 2006;17:ii58–60.

[6] The Elderly Lung Cancer Vinorelbine Italian Study Group. Effects of vinorelbine on quality of life and survival of elderly patients with advanced non-small-cell lung cancer. J Natl Cancer Inst 1999;91: 66–72.

[7] Gridelli C, Aapro M, Ardizzoni A, et al. Treatment of advanced non-small-cell lung cancer in the elderly: results of an international expert panel. J Clin Oncol 2005;23:3125–37.

[8] Frasci G, Lorusso V, Panza N, et al. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small-cell lung cancer. J Clin Oncol 2000;18:2529–36.

[9] Gridelli C, Perrone F, Gallo C, et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. J Natl Cancer Inst 2003;95:362–72.

[10] LeCaer H, Delhoume JY, Thomas PA, et al. Multicenter phase II trial of carboplatin/vinorelbine in elderly patients with advanced non-small-cell lung cancer efficacy and impact on quality of life: Groupe Francais de Pneumo-Cancerologie Study 9902. Clin Lung Cancer 2005;7:114–20.

[11] Neubauer MA, Garfield DH, Kuerfler PR, et al. Results of a phase II multicenter trial of weekly docetaxel and gemcitabine as first-line therapy for patients with advanced non-small-cell lung cancer. Lung Cancer 2005;47:121–7.

[12] Dy S, Sharkey M, Herbert P, et al. Comorbid illnesses and health care utilization among medicare beneficiaries with lung cancer. Crit Rev Oncol Hematol 2006;59:218–25.

[13] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245–51.

[14] Frasci G. Chemotherapy of lung cancer in the elderly. Crit Rev Oncol Hematol 2002;41:349–61.

[15] Firat S, Bousamra M, Gore E, et al. Comorbidity, and KPS are independent prognostic factors in stage I non-small-cell lung cancer. Int J Radiat Biol Phys 2002;52:1047–57.

[16] Hainsworth JD, Burris III HA, Greco FA. Weekly docetaxel as a single agent and in combination with gemcitabine in elderly and poor performance status patients with advanced non-small-cell lung cancer. Semin Oncol 2001;28:21–5.

[17] Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 2000;92:205–16.

[18] Spitzer WO, Dobson AJ, Hall J, et al. Measuring the quality of life of cancer patients: a concise QL-index for use by physicians. J Chronic Dis 1981;34:585–97.

[19] Hollen PJ, Gralla RJ, Kris MG, et al. Measurement of quality of life in patients with lung cancer in multicenter trials of new therapies psychometric assessment of the Lung Cancer Symptom Scale. Cancer 1994;73:2087–98.

[20] Gehan EA. The determination of the number of patients required in a preliminary and a follow-up trial of a new chemotherapeutic agent. J Chronic Dis 1961;13:346–53.

[21] Chen YM, Preng RP, Lin WC, et al. Phase II study of docetaxel and gemcitabine combination chemotherapy in non-small-cell lung cancer patients failing previous chemotherapy. Am J Clin Oncol 2002;25:509–12.

[22] Kouroussis C, Mavroudis D, Kakolyris S, et al. High incidence of pulmonary toxicity of weekly docetaxel and gemcitabine in patient with non-small-cell lung cancer: results of a dose-finding study. Lung Cancer 2004;44:363–8.

[23] Littlewood TJ, Bajetta E, Nortier JW, et al. Effects of epoetin alfa on hematologic parameters and quality of life in cancer patients receiving nonplatinum chemotherapy: results of a randomized, double-blind, placebo-controlled trial. J Clin Oncol 2001;19:2865–74.

[24] Giorgio CG, Pappalardo A, Russo A, et al. A phase II study of carboplatin and paclitaxel as first line chemotherapy in elderly patients with advanced non-small-cell lung cancer (NSCLC). Lung Cancer 2006;51:357–62.

[25] Quoix E, Breton JL, Ducolone A, et al. First line chemotherapy with gemcitabine in advanced non-small-cell lung cancer elderly patients: a randomized phase II study of 3-week versus 4-week schedule. Lung Cancer 2005;47:405–12.

[26] Hirsh V, Latreille J, Kreisman H, et al. Sequential therapy with vinorelbine followed by gemcitabine in patients with metastatic non-small-cell lung cancer (NSCLC) performance status (PS) 2 or elderly with comorbidities—a multicenter phase II trial. Lung Cancer 2005;49:117–23.

[27] Santo A, Genestri G, Terzi A, et al. Gemcitabine and vindesine in advanced non-small-cell lung cancer: a phase II study in elderly or poor performance status patients. Lung Cancer 2006;53: 355–60.

[28] Pujol JL, Breton JL, Gervais R, et al. Gemcitabine–docetaxel versus cisplatin–vinorelbin in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. Ann Oncol 2005;16:602–10.

[29] Kosmidis P, Mylonakis N, Nicolaides C, et al. Paclitaxel plus carboplatin versus gemcitabine plus paclitaxel in advanced non-small-cell lung cancer: a phase III randomized trial. J Clin Oncol 2002;20:3578–85.

[30] Laack E, Dickgreber N, Muller T, et al. Randomized phase III stydy of gemcitabine and vinorebin versus gemcitabine, vinorelbin, and cisplatin in the treatment of advanced non-small-cell lung cancer: from the German and Swiss Lung Cancer Study Group. J Clin Oncol 2004;22:2348–56.

[31] Bria E, Cuppone F, Ciccarese M, et al. Weekly docetaxel as second line chemotherapy for advanced non-small-cell lung cancer: meta-analysis of randomized trials. Cancer Treat Rev 2006;32:583–7.

[32] Bhatia S, Hanna N, Ansari R, et al. A phase II study of weekly gemcitabine and paclitaxel in patients with previously untreated stage IIIB and IV non-small-cell lung cancer. Lung Cancer 2002;38: 73–7.

[33] Dujon C, Azarian R, Azarian V, et al. Lung cancer in the elderly: performance status and/or geriatric indice? Rev Mal Respir 2006;23: 307–18.

[34] Read W, Tierney R, Page N, et al. Differential prognostic impact of comorbidity. J Clin Oncol 2004;22:3099–103.

[35] Extermann M, Meyer J, McGinnis M, et al. A comprehensive geriatric intervention detects multiple problems in older breast cancer patients. Crit Rev Oncol Hematol 2004;49:69–75.

[36] Extermann M, Aapro MS, Bernabei R, et al. Use of comprehensive assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol 2005;55:241–52.
[37] Maione P, Perrone F, Gallo C, et al. Pretreatment quality of life and functional status assessment significantly predict survival of elderly patients with advanced non-small-cell lung cancer receiving chemotherapy: a prognostic analysis of the multicenter Italian lung cancer in the elderly study. J Clin Oncol 2005;23:6865–72.

Biography

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