

## Cytostatic chemotherapy for small cell lung cancer in patients of age 75 years or older

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*Eleven patients of age 75 years or older with histologically and/or cytologically proven small cell lung cancer (SCLC) were treated at our institution during the period of 5 years 1990-1994.*

*Patients characteristics: 10 men, 1 woman, age: median: 77, range: 75-82 years, performance status WHO  $\leq$  3.*

*Treatment: different treatment schedules were used according to patients status and comorbidity. Single drug therapy with teniposide or etoposide was used in five patients, in six patients further cytostatics (mostly carboplatin) were used in addition.*

*Results: response rate after 2 courses of therapy: complete response: 1 (9%), partial response: 5 (45%), stable disease: 3 (27%), progression: 2 (18%), survival time: median: 7.5, range: 1-32 + months, adverse effects: except for 3 leukopenias (2x WHO grade 3, 1x WHO grade 4) no serious adverse effects.*

*Conclusion: currently available cytostatics for SCLC, especially epipodophyllotoxins alone or in combination with carboplatin, seem to be effective and (with adequate premedication) well tolerated even in very old patients.*

*Key words: lung neoplasms-drug therapy; carcinoma, small cell; antineoplastic agents; aged*

### Introduction

Small cell lung cancer accounts for approximately 25% of all cases of lung cancer.<sup>1</sup> Cytostatic chemotherapy is the standard treatment modality as initial therapy and favorably influences both quality and quantity of survival. However, very old patients are regarded as a poor candidates for aggressive combination chemothera-

py. Chronological age per se should not, in our view, exclude patient from the standard protocol of treatment. Most of these patients, if not all, may have, however, comorbid conditions such as chronic obstructive lung disease, congestive heart failure, coronary artery disease, or others, that will influence the decision of chemotherapy. Further, there is an age-related reduction in creatinine clearance.<sup>2</sup> The wishes and expectations of the elderly patient may differ and must be considered before treatment decision as well.

There are only a few data in the literature about the cytostatic chemotherapy for small cell lung cancer in elderly patients and in fact

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**Table 1.** Patients characteristics.

No. of patients	11
Male	10
Female	1
Age (yrs)	
median	77
range	75–82
Performance status	
WHO 1	3
WHO 2	5
WHO 3	3
Disease stage	
Limited disease	5
Extensive disease	6

none aimed specifically at the very old patients. The aim of our retrospective study was to assess the results of cytostatic chemotherapy for small cell lung cancer in 75 years or older patients, i. e. the patients who are considered to be very old.

### Patients and methods

Eleven patients of 75 years or older with histologically and/or cytologically proven small cell lung cancer were treated at our institution during the period of 5 years: 01. 01. 1990 – 31. 12. 1994. Characteristics of the patients are shown in Table 1.

By the start of chemotherapy 5 patients were considered to have limited disease (LD), 6 extensive disease (ED) – defined as a tumor dissemination beyond the hemithorax and its regional node drainage (mediastinal, scalene and supraclavicular).

Different cytostatic treatment schedules were used according to patients status and comorbidity. Single drug therapy with epipodophyllotoxins – teniposide or etoposide – was used in five patients, in six patients further cytostatics (mostly carboplatin, in one case cyclophosphamide) were used in addition. The overview of treatment schemes most often used in our patients is in Table 2. Chemotherapy was planned for at least 2 courses and maximum 6 courses in responders. Chest radiotherapy was suggested to 2 patients with LD after the chemotherapy, but it was accepted only by 1 patient.

**Table 2.** Therapeutic protocols.

No. Drug	Daily dose mg/m <sup>2</sup>	Admini- stration route	Day	Frequency
1. Etoposide	150	p. o	1–5	3 weeks
2. Etoposide	120	i. v.	1–3	3 weeks
3. Teniposide	30	i. v.	1–5	15 days
4. Etoposide	120	i. v.	1–3	3 weeks
Carboplatin	300	i. v.	1	

Patients evaluation before therapy included a history and physical examination, complete blood count, urinalysis, electrolyte levels, chemical survey, roentgenograms and ultrasound investigation. These investigations were repeated before each course of therapy. CT was used only selectively, bone radionuclide scans were used in the same manner.

A complete response was defined as the disappearance of all evidence of tumor for at least 4 weeks. A partial response was defined as a 50% or greater decrease in the sum of the products of the diameters of all measured lesions persisting at least 4 weeks. No lesion could increase in size and no lesion could appear. Progressive disease was defined as any increase greater than 25% in the sum of the products of diameters of any observed lesion or as the appearance of any new lesion. Survival was calculated from the start of chemotherapy.

### Results

#### Response data

The response data after 2 courses of therapy are shown in Table 3.

The overall response rate was 6/11 (54%). The response rate in the group of patients treated with single drug therapy – teniposide or etoposide – was 3/5 (60%), in the group of patients treated with combination of cytostatics: 3/6 (50%).

Eleven patients received total 32 courses of chemotherapy, mean 2.9 courses per patient, range: 1 – 6 courses. Despite our intention to administer at least 2 courses of chemotherapy, 2 patients received only 1 course of treatment.

**Table 3.** Response data and survival.

No. of patients	11
Complete response	1 (9%)
Partial response	5 (45%)
Stable disease	3 (27%)
Progression	2 (18%)
Overall response	6 (54%)
Survival (month)	
median	7.5
range	1–32 +
Follow-up (month)	
median	7.5
range	1–32

This resulted from rapidly progressive disease in one patient and from overall somatic deterioration in second patient by progressive cancer disease. These patients were included into the analysis of the results, as well as one patient with chest radiotherapy followed after 4 courses of chemotherapy with teniposide (the survival time in this last patient was 9 months).

### Toxicity

Except for 3 leukopenias (WHO grade 3: 2x, WHO grade 4: 1x) no serious side effects were observed. All patients received antiemetics, mostly oral ondansetron alone or in combination with intravenous dexamethason, given as a standard before the chemotherapy and repeated if needed, so there was virtually no vomitus.

### Discussion

Elderly patients were frequently excluded from clinical trials until recently,<sup>3</sup> so it is not surprising that the data in the literature about the treatment of small cell lung cancer in this group of patients are limited. Smit et al.<sup>4</sup> reported overall response rate 71% in 35 patients older than 70 years treated with oral etoposide 800 mg/m<sup>2</sup> over 5 consecutive days. Toxicity was minimal and there were no hospitalizations needed for drug-related toxicity. Carney et al.<sup>5</sup> observed with the same treatment scheme overall response rate 79% in a group of 53 patients in the age 70 years or older.

Bork et al.<sup>6</sup> observed response rates 77% and 66% respectively in the comparative study of teniposide and etoposide in a dose 70 mg/m<sup>2</sup> for 5 days for both drugs and median survival time 11 v 8.5 months in 92 patients of age 70 years or older. Other authors<sup>7,8</sup> have reported response around 50% in elderly patients treated with teniposide as single drug therapy, but Cerny et al.<sup>8</sup> reported high toxic death rate 5 of 30 in their group of patients with a fixed dose of teniposide 100 mg/m<sup>2</sup> every 3 weeks.

Bishop<sup>9</sup> and Raghavan et al.<sup>10</sup> studied the outcome in 26 patients treated with carboplatin + etoposide combination who were aged 70 years or older. An objective response was seen in 88% of patients. Neutropenia and thrombocytopenia were seen more often than in younger patients, but none of the elderly patients had infective or bleeding sequelae.

The overall response rate to the chemotherapy seen in our patients in the age of 75 years or older was 54% – similar to the results of the other, above mentioned authors. Median survival time was 7.5 months after the start of chemotherapy. In one patient the long – term survival has been achieved and the patient continues to live in good overall status 32 months after the start of chemotherapy i. e. 28 months after finishing 4 courses of carboplatin/etoposide chemotherapy. The toxicity of chemotherapy in our group of patients as a whole was acceptable.

Considering the fact, that the median survival time for untreated patients with small cell lung cancer is only 2 or 7 weeks for extensive or limited disease respectively,<sup>11</sup> we may conclude, that the currently available cytostatics, especially epipodophyllotoxins alone or in combination with carboplatin, seem to be effective and with adequate premedication well tolerated even in very old patients.

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