Eur J Cancer Clin Oncol, Vol. 23, No. 5, pp. 541–544, 1987.
Printed in Great Britain

0277-5379/87$3.00+0.00

Long-term Survival in Small Cell Carcinoma of the Lung

CINTA PALLARES, ROMÁ BASTUS, JUAN JOSÉ LOPEZ and LUIS DE ANDRES

Medical Oncology Unit, Oncology Department, Hospital Santa Creu i Sant Pau, Universitat Autónoma de Barcelona, Barcelona

Abstract—*We analyzed the long-term survivors in a group of* 255 *patients with newly diagnosed small cell carcinoma of the lung (SCCL) between January* 1978 *and July* 1983. *Long-term survivors were defined as those patients free of cancer* 2 years *after initiation of therapy. Only* 6 *patients* (2.5%) *were free of disease at this time. Two patients relapsed at* 29 *and* 40 months *from the start of chemotherapy. Both patients were retreated with chemotherapy, and one of them achieved a complete response. Despite the increase in median survival in SCCL with chemotherapy over the past* 10 years, *long-term prognosis remains very poor employing standard treatments.*

INTRODUCTION

COMBINATION chemotherapy has resulted in markedly increased response rates and survival in small cell carcinoma of the lung (SCCL); nonetheless, relapse occurs in most patients, and death a few months later is the rule. Median survival is around 12 months [1] and to date has not increased with new therapeutic strategies.

Most reports on the treatment of SCCL describe short term follow-up with several therapeutical regimes, utilizing combination chemotherapies with or without radiation therapy; however, few have focused on long-term survivors or morbidity in these patients. In fact, there is no agreement about the definition of "the long-term survivor"; some authors have indicated a specific survival period, generally between 18 and 60 months (2–4); whereas others believe that patients must remain free of disease for as long as 2 years after initiation of therapy (5–7).

In this paper we describe the long-term survivors in a group of 225 patients with SCCL, defined as those who are disease-free 24 months from start of treatment.

MATERIALS AND METHODS

Two hundred and twenty-five patients with histologically confirmed SCCL with no previous treatment were referred to our Oncology Department from January 1978 through July 1983. Median age was 60 years; 3 patients were 70 or older. Initial staging included history and physical examination, evaluation of performance status using the Karnofsky scale (KPS), complete blood count, serum chemistries and chest roentgenogram. When clinical metastases were suspected, brain or body computer tomographic scan and bone or hepatic scan were done. In a clinical trial with 34 patients, systematic staging with hepatic scan, computer tomographic scan of the brain as well as a bilateral bone marrow biopsy were performed. All patients were staged as having either limited disease or extensive disease, based on the criterion developed by the Veterans Administration Lung Cancer Study Group [8].

Table 1. *Characteristics of all patients*

Total no. of patients	225
Median age at diagnosis	60
Stage of disease	
limited	61 (27%)
extensive	164 (73%)
Karnosfsky performance status	
80–100	85 (38%)
60–70	102 (45%)
≤50	3 (15%)
unknown	5 (2%)

Patient characteristics are summarized in Table 1. The chemotherapy given can be divided into two periods: the first, from January 1978 through 1982 approximately, 116 patients received cyclophosphamide (500 mg/m^2) intravenously on days 1 and 21, methotrexate (25 mg/m^2) intravenously weekly and carmustine (50 mg/m^2) orally on day 1 and 42 (CMC) and 34 patients received an induction

Accepted 7 November 1986.
Reprint requests to: Cinta Pallares, Medical Oncology Unit, Department of Oncology, Hospital Santa Creu i Sant Pau, Av. S. Antoni Ma Claret, 167, 08025 Barcelona, Spain.

Table 2. Treatment and number of long-term survivors in each group

Chemotherapy*	Number of patients	Chest radiation patients	Long-term survivors
CMC	116	25	3
CMC + VAP	34	7	2
CYCLO+VP-16 ± ADRIA	59	18	1
No treatment	16	–	–
Total	225	50	6

* CMC = Cyclophosphamide, methotrexate, lomustine
VAP = Vincristine, doxorubicin, procarbacine
CYCLO = Cyclophosphamide
ADRIA = Doxorubicin

regimen consisting of two cycles of cyclophosphamide (1000 mg/m^2) intravenously on days 1 and 21, methotrexate (50 mg/m^2) intravenously weekly and carmustine (100 mg/m^2) orally on day 1 and repeated on day 42 followed by vincristine (1.4 mg/m^2) on day 1, doxorubicin (50 mg/m^2) on day 1 and procarbazine (100 mg/m^2 per day) orally on days 1–7 inclusive (VAP), alternated with CMC. In the second period, from 1982 to July 1983, 44 patients received cyclophosphamide (100 mg/m^2) intravenously and doxorubicin (45 mg/m^2) on day 1, adding intravenous VP-16 (50 mg/m^2) on days 1 to 5 inclusive, repeating the whole regimen every 3 weeks (CAVP-16). In 15 additional patients doxorubicin was excluded due to advanced age or cardiac disease (Table 2). Sixteen patients were not given chemotherapy owing to low performance status.

Patients with limited disease received chest radiotherapy (4000–4500 rads) usually after four to six courses of chemotherapy. Combination chemotherapy was continued following radiation therapy over a 12 month period. None of the patients received prophylactic whole brain radiotherapy. Initial staging procedures were repeated in patients clinically free of disease at the end of treatment; if results were normal treatment was discontinued.

RESULTS

Overall survival in shown in Figure 1. The number of patients with discontinuation or modification of cytotoxic agent dosages due to chemotherapy toxicity are shown in Table 3. Basically, cytostatic regimen modifications were due to hematologic toxicity in the CMC and CAVP-16 group, and to gastrointestinal toxicity in the VAP group.

Only 6 patients (2.5%) were free of disease 24 months from the initiation of therapy; 5 were initially staged as having limited disease and 1 as having extensive disease. At diagnosis, all patients had a KPS of > 60. Patient characteristics are summarized in Table 4.

All 5 patients with limited disease were free of disease at the end of the study; follow-up was 24, 38, 50 and 63 months respectively from the start of treatment. One patient presented an apical infiltrate in the other lung 28 months following completion of therapy. Bronchoscopy was normal but percutaneous needle aspiration was positive for SCCL; staging was not done. He was retreated with combination chemotherapy followed by chest irradiation, and complete response was achieved. At present he is alive and disease-free 63 months from initiation of the first treatment and 23 months from the start of the second.

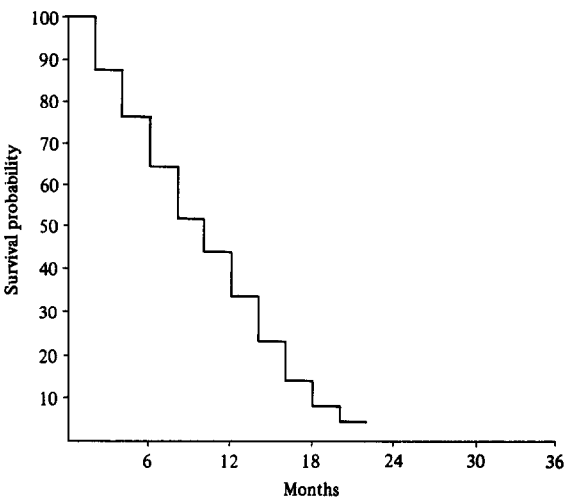

Fig. 1. Overall survival

The only patient staged as having extensive disease had a bilateral supraclavicular lymph node involvement; classification was based on hepatic scan, computer tomographic scan of the brain and bilateral bone marrow biopsy results. Given this localization chest radiotherapy was done. At the end of treatment a complete response was observed; however 29 months after initiation of chemotherapy he relapsed with a pleural effusion. Pleural biopsy was positive and he was retreated with combination chemotherapy. At present, 52 months from diagnosis, he is alive with disease.

Table 3. Severe toxicity in all patients treated with chemotherapy

Treatment regimen	Number of patients	Modification of cytotoxic treatment	Discontinuation of chemotherapy treatment	Treatment related-deaths
CMC	116	30 (26%)	14 (12%)	3 (2.5)
CMC+VAP	34	15 (44%)	4 (11%)	—
CYCLO+VP-16 ± ADRIA	59	15 (25%)	2 (3%)	3 (3%)
Total	209	60 (29%)	20 (10%)	6 (3%)

* CMC = Cyclophosphamide, methotrexate, lomustine
VAP = Vincristne, doxorubicin, procarbacine
CYCLO = Cyclophosphamide
ADRIA = Doxorubicin

Table 4. Characteristics, treatment and follow-up of the long-term survivors

Patient	Age	Karnosfsky performance status	Stage	Chemotherapy*	Chest radiation (Gy)	Follow-up (months)
1	67	100	Limited	CMC	–	63
2	55	80	Limited	CMC	40	57
3	46	80	Extensive	CMC+VAP	40	52
4	45	70	Limited	CMC+VAP	41	50
5	70	90	Limited	CMC	40	38
6	65	90	Limited	CAVP-16	40	24

* CMC = Cyclophosphamide, methotrexate, lomustine
VAP = Vincristine, doxorubicin, procarbacine
CAVP-16 = Cyclophosphamide, doxorubicin, VP-16-213

DISCUSSION

SCCL belongs to a group of tumors sensitive to treatment with chemotherapy (total response around 80%); thus it is disturbing to observe that only 6 of 225 patients were free of disease 24 months after initiation of therapy. When compared to other reports the low incidence of patients with limited disease in this series (61/225, 27%) is noteworthy, given that no systematic exhaustive staging was done.

Unlike other studies, we included all newly diagnosed patients with small cell lung cancer referred to our Department rather than only those patients who met specific inclusion-criteria; therefore, we evaluated patients over 70 years, with KPS < 60, brain metastasis present at diagnosis as well as a group of patients who did not receive chemotherapy because of low performance status. It is felt that this approach is more realistic and allows an accurate overview of the natural history as well as the overall treatment effort that SCCL represents.

When we analyze only patients with limited disease, the percentage of long-term survivors is lower than that reported elsewhere; only 8% (5/61) were free of cancer 24 months after the start of chemotherapy, whereas based on other reports which used the same criteria, 15–20% are expected to be long-term survivors [1].

One patient had a lung recurrence 40 months after initial treatment. Complete response was achieved after retreatment with chemotherapy and radiation therapy. Late recurrence is not unusual, relapses have been reported as long as 74 and 96 months after the start of chemotherapy [3, 5].

Batist has reported a group of 6 patients with late recurrence, 4 of whom had responses after being retreated with chemotherapy [9]; this suggests that although limited in number, these patients could have a higher response rate than that of others with early recurrence.

In this study, like in others, most long-term survivors were patients with limited disease; nonetheless, an analysis of other prognostic factors which might improve the identification of long-term survivors can not be ventured owing to our low sample size.

REFERENCES

1. Aisner J, Alberto P, Bitran J, *et al.* Role of chemotherapy in small cell lung cancer: a consensus report of the International Association for the Study of Lung Cancer Workshop. *Cancer Treat Rep* 1983, **67**, 37–43.
2. Hansen M, Hansen H, Dombernowsky P. Long-term survival in small cell carcinoma of the lung. *JAMA* 1980; **244**, 247–250.
3. Vogelsang G, Abeloff M, Ettinger D, *et al.* Long-term survivors of small cell carcinoma of the lung. *Am J Med* 1985, **79**, 49–56.
4. Livingston R, Stephens R, Bonnet J, *et al.* Long term survival and toxicity in small cell lung cancer. *Am J Med* 1984, **77**, 415–417.
5. Johnson B, Ihde D, Bunn P, *et al.* Patients with small cell lung cancer treated with combination chemotherapy with or without irradiation. *Ann Intern Med* 1985, **103**, 430–438.
6. Volk S, Mansour R, Gandara D, *et al.* Morbidity in long-term survivors of small carcinoma of the lung. *Cancer* 1984, **54**, 25–27.
7. Ginsberg S, Comis R, Gottlier A, *et al.* Long-term survivorship in small cell anaplastic lung carcinoma. *Cancer Treat Rep* 1979, **63**, 1347–1349.
8. Zelen M. Keynote address on biostatistics and data retrieval. *Cancer Chemother Rep* 1973, part 3, **4**(2), 31–42.
9. Batist G, Ihde D, Zabell A, *et al.* Small cell carcinoma of lung: reinduction therapy after late relapse. *Ann Intern Med* 1983, **98**, 472–74.