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Short Report

VP16-213 Combined with Cis-Platinum (CDDP) in the Treatment of Small Cell Carcinoma of the Lung (SCLC)

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Introduction

The overall 5-year survival rate of patients with bronchogenic carcinoma remains at 8–10% [12] and 50% of the patients have recognized extrapulmonary metastases at the time of diagnosis [3]. Small cell carcinoma, which accounts for about 20% of all lung cancers [11] is usually in an advanced stage, but this lung tumor is the most sensitive to chemotherapy [10].

The current study was undertaken to determine the rate of response to combination chemotherapy using VP16-213 and CDDP.

Patients and Methods

Twelve patients with advanced SCLC have been entered in this trial. Characteristic of the patients are listed in Table 1. Of the 12 patients admitted in the study, two were non-evaluable.

Eleven were men, one woman. Two men were non-evaluable. The mean age of evaluable patients was 51 with a range from 34–63.

The patients had a life expectancy longer than two months and had a performance status superior to 40 in the Karnofsky scale with a range from 40–70.

Table 1. Patient data

No. of patients entered	12
No. of non-evaluable patients	2
No. of evaluable patients	10
Mean age, in yr. evaluable patient	51
(range)	(34–63)
Male/female ratio. Evaluable patient	9/1
Mean performance st. (Karnofsky sc.)	60
(range)	(40–70)
Previous treatment	
Chemotherapy	2
Radiotherapy	1
Radiotherapy–chemotherapy	5
None treatment	2

Eight patients had been treated previously with different therapies: two chemotherapy, one radiotherapy, and five radiotherapy and chemotherapy. Four patients had received no treatment. The study parameters included physical examination, chest x-ray, fibrobronchoscopy, bone, liver, and brain scans. Blood study: WBC and platelet count, hemoglobin, urea nitrogen, liver function tests, serum creatinine, and serum electrolytes.

Creatinine clearance was performed also.

Eligibility required a microscopic diagnosis, objectively measurable disease, creatinine clearance superior to 70 ml./minute, performance status superior to 40 (Karnofsky scale) and acceptable hematologic status (WBC count superior to 4,000 and platelet count superior to 125,000).

CDDP was administered intravenously (i.v.) after hydration and mannitol-induced diuresis at 100 mg/m^2 on day 1. VP16-213 was given orally at 130 mg/m^2 on days 2, 3, 4, and 5.

Chemotherapy was repeated every 21 days and a complete blood count, serum creatinine and liver function tests were repeated periodically to monitor toxicity related to treatment. Patients were evaluated after two courses of therapy.

Complete responder patients received prophylactic whole brain radiation after two courses of treatment.

Response criteria were defined as follows:
Complete remission (CR) – Disappearance of all evidence of disease for at least one month.

Partial remission (PR) – A decrease of 50% or more of all measurable disease, for a minimum of one month.

No Change (NC) – No appreciable change in measurable lesions. Patients whose measurable lesions regressed less than 50% during the course of the treatment were considered "no change".

Progression (PG) – Increase of any of the measurable lesions or the appearance of new ones.

Clearing of pleural effusion was not considered as evidence of remission.

Results

Twelve patients entered in this trial, but 2 were invalidated at the end of the first course of therapy by progression of the disease. The results are shown in Table 2.

The remaining ten patients form the basis for this report. There were five complete remissions and

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Table 2. Results of treatment

No. of Patient	CR	PR	NC
10	5	3	2
%	50	30	20

Table 3. Toxicity

Nausea and vomiting	10 (100%)
WBC less than 2,500	4 (40%)
Alopecia	9 (90%)
Renal toxicity	1 (10%)

three partial with an overall response rate of 80%. Two patients showed no change response. The duration of the eight good responses varied from 2.5 months to 12+ months.

The median duration of PR was 5 months and for the it CR; has not been reached.

The median survival of the eight responders from start of treatment is 9.8+ months.

Toxicity

Toxicity is listed in Table 3.

Nausea and vomiting on the first day of therapy were almost universal, usually began about 2 h, after the injection of CDDP and persisted for 2–8 h. Prolonged nausea and vomiting were uncommon.

Alopecia appeared in nine patients. Leukopenia occurred frequently after the initial treatment.

The mean leucocyte nadir of these ten patients was 3,200 on day 14, but WBC less than 2,500 was seen in four of ten patients.

Thrombocytopenia (platelets less than 100,000) was not seen.

Renal toxicity (creatinine clearance below 60 ml/min) was seen in only one patient.

Anemia was generally not a clinical problem. Recovery of low blood counts occurred rapidly in most instances.

Ototoxicity was not seen.

Discussion

SCLC is a rapidly fatal disease and if untreated it has a median survival from diagnosis to death of 3 months. [6]. The use of single chemotherapy produces a tumor response in at least 30% of the patients [7], and combination chemotherapy produces objective response rates exceeding 75% and median survivals of 1 year or more for both limited and disseminated disease [4].

VP16-213 produces response rates higher to 40% [5, 9] even in previously treated patients with a good tolerance. CDDP produces a tumor response rate in up to 70% with tolerable toxicity [2].

Encouraging results have been obtained in the treatment of SCLC with a combination of VP16-213 and CDDP [8] and alternating chemotherapy does not appear effective in increasing the frequency of remissions [1].

The preliminary results of this trial have demonstrated that the VP16-213 and CDDP combination produces an objective response rate of 80% the in a small series of patients.

Overall drug toxicity was tolerable and no case of definite drug related death was observed. Damage to the kidney was not seen.

We conclude that these preliminary results show that this regimen has produced promising results in the treatment of patients with advanced SCLC without any noteworthy toxicity.

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