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Short Report

VP16-213 and Cyclophosphamide in non Oat Cell Bronchogenic Carcinoma

L. Morasca[1], S. Marsoni[1], M. Brambilla Pisoni[2], E. Piazza[2], G. Vago[2], W. Casali[3], R. Cogo[3], C. Bianchi[3], and R. Scapaticci[3]

[1] Istituto di Ricerche Farmacologiche M. Negri, Via Eritrea, 62, I-20157 Milan
[2] Sacco H. Clin. Int. Med. Univ., Via G. B. Grassi 74, I-20157 Milan
[3] Ornago H., Via C. Battisti 23, I-20059 Vimercate, Italy

Summary. *Thirty-two patients with by non oat cell bronchogenic carcinoma were admitted to a protocol including Cyclophosphamide (CTX) 1,000 mg/m² i.v. day 1, VP16-213 200 mg/m² p.o. day 1–3, every 3 weeks.*

Partial remissions were seen in 2 of 27 evaluable patients; 16 of 27 showed no change. Mean survival was 36.4 weeks, median survival was 38 weeks.

Introduction

The North Milan Cooperative Group has studied two-drug combination chemotherapy with cyclophosphamide and VP16-213, for non-oat-cell bronchogenic carcinoma. In the literature the efficacy of VP16-213 is described for small cell carcinoma, for squamous cell, and adenocarcinoma of the lung, and in a variety of hematological malignancies [2–4]. VP16-213 appeared to be less toxic than other compounds. Nausea and vomiting are relatively infrequent and mild [5]. The aim of this protocol was to evaluate the clinical safety and therapeutic effectiveness of this chemotherapy combination.

Patient Population

Between February 1980 and March 1981, 32 patients entered this study. All patients had objectively measurable disease and histological confirmation of the diagnosis of non-small-cell bronchogenic carcinoma.

The distribution of patients by cell type was 24 squamous cell carcinoma, 8 adenocarcinoma. Nine patients had stage II; 23 patients stage III (eight patients M_1). All patients had performance status > 50, by Karnofsky's scale; no previous radiotherapy or chemotherapy; estimated survival more than 3 months were required.

Send offprint requests to L. Morasca at the above address

Before starting chemotherapy, all patients underwent complete history and physical examination and routine laboratory evaluation. A platelet count of $> 150{,}000/mm^3$, WBC $> 4{,}000/mm^3$ and normal renal and hepatic function were required.

Drug dosage schedule was: cyclophosphamide (CTX) 1,000 mg/m² i.v. day 1, VP 16-213 200 mg/m² p.o. day 1–3, every 3 weeks. Adequate treatment required a minimum of three cycles of chemotherapy. Response criteria were defined as: complete remission (CR) – disappearance of all evidence of disease; partial remission (PR) – 50% reduction of all measurable lesions; no change (NC) – objective tumor reduction 30%, but less than that required for a PR; progression (P) – objective increase in measurable disease, or appearance of new tumor lesions.

Appropriate dose modifications were made for hematological and gastrointestinal toxicity. Treatment was stopped for WBC $< 2{,}000/mm^3$ and platelet count $< 50{,}000/mm^3$ or for serious gastrointestinal intolerance.

The patients with PR or NC received the same chemotherapy as maintenance every month.

Results

After three cycles of chemotherapy, patients were evaluated for response. Twenty-seven of thirty-two patients were evaluable. Two patients were excluded because they had received less than three cycles of therapy, and three died during therapy. Two of these 27 patients obtained an objective response (PR), 15 of 27 patients were no change (NC), and 10 of 27 were in overt progression (P). Duration of PR ranged from 6–7 months.

All these cases were evaluable for survival. Fifteen of twenty-seven patients died: ten from disease progression and five, after initial stabilisation of the disease, died from overt progression at two cycles of maintenance.

After 1 year of treatment 12 of 27 patients are alive.

Table 1 summarizes the patients' characteristics and response from the start of treatment.

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Table 1. Characteristics response and survival of patients

Cell type	Patient no.	Evaluable	Response			Not evaluable
			PR	NC	P	
Squamous	22	19	2	10	7	3[a]
Adenoca	8	8	–	5	3	–
Unclassified	2	–	–	–	–	2[b]
Total	32	27	2	15	10	5
MST (weeks)	–	38	–	49	28	–

[a] Death within 3 months
[b] Refused therapy

The mean survival time for the whole group was 36.4 weeks, the median survival time (MST) being 38 weeks. The NC patients achieved an MST of 49 weeks, and P patients an MST of 28 weeks.

Toxicity was limited: mild nausea and vomiting in three patients, anorexia in two, alopecia in 14, mild leukopenia in one patient.

Suspension of therapy was never required.

Discussion

In our study, the combination of VP16-213 and Cyclophosphamide induced tumor regression in 7% of treated patients.

We cannot consider as a response to therapy the stabilisation (55%) observed. Ten patients (37%) had definite progression.

The mild toxicity of VP16-213 permits the use of the drug in combination with cyclophosphamide. In this study toxicity was acceptable, with only mild nausea, vomiting and anorexia; myelosuppression occurred in only one patient.

The combination of CPA and VP16-213 achieved a tumor response similar to those obtained with other chemotherapeutic regimens. The median survival of patients was also not significantly different from the median survival time of patients treated with other multidrug schedules [1, 6].

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