Eur J Cancer Clin Oncol, Vol. 22, No. 8, pp. 983–985, 1986.
Printed in Great Britain.

0277-5379/86$3.00+0.00
Pergamon Journals Ltd.

Vindesine and Mitomycin C in Inoperable Non-Small Cell Lung Cancer

JOHN MAIN,* ROLAND A. CLARK† and ANDREW HUTCHEON‡

**Department of Medicine, Aberdeen Royal Infirmary, †Department of Thoracic Medicine, University of Dundee and ‡Departments of Medicine and Medical Oncology, Aberdeen Royal Infirmary, U.K.*

Abstract—*Twenty-nine patients with inoperable non-small cell lung cancer were treated as out-patients with vindesine and mitomycin C. Eight patients had a complete response, and nine a partial response. Response was generally associated with either stable or improving ECOG and symptom scores. The incidence of serious side-effects was low — only two patients' white cell count fell below* 3000 cells/mm^2, *only one patient's platelet count fell below* 100,000 cells/mm^2, *and two patients developed vomiting associated with treatment. The combination of vindesine and mitomycin C appears to be effective in the treatment of inoperable non-small cell lung cancer. Side effects were generally well tolerated and allowed out-patient treatment.*

INTRODUCTION

FEW chemotherapeutic agents exhibit well-documented activity in inoperable non-small cell lung cancer (NSCLC). *Cis*-platinum, mitomycin C and vindesine are three of the more active [1]. Although the combination of vindesine and cisplatin has produced response rates in excess of 40% in patients with metastatic disease, the incidence of vomiting was high and precluded out-patient therapy [2]. The objects of this study were to evaluate the effects of out-patient treatment with vindesine and mitomycin C and to assess associated toxicity.

PATIENTS AND METHODS

Twenty-nine patients, 19 male and 10 female, aged 26–72 (mean 58), were entered into the study which had ethical committee approval, and informed consent was obtained from all patients. All had histologically proven, inoperable NSCLC which was objectively measurable; an ECOG status of 0–2; and had no prior chemotherapy; two patients had received prior radiotherapy. Seventeen patients had extensive disease and 12 patients, limited disease [3]. The quality of life of patients on treatment was assessed by monitoring side effects, symptom score and ECOG status for the duration of treatment.

Most patients had three or more courses of mitomycin C, 10 mg/m^2 i.v. on Day 1 with vindesine 3 mg/m^2 i.v. on Days 1 and 8, courses being repeated at 28-day intervals, although five patients had two and one, one course. All patients were included in the analysis. Tumour response was graded by standard criteria [4] and duration of response was defined as the time from initiation of treatment to disease progression. Response was not confirmed by bronchoscopy.

RESULTS

Response to therapy is summarized in Table 1.

Eight patients (28%) had a complete response — three of six with adenocarcinoma and 5 of 19 with squamous carcinoma. Complete response occurred after three courses in five patients and after four courses in three patients. This response lasted from 4 to 13 months ($\bar{x}$ = 7.6). Nine patients (31%) had a partial response. In responding patients, sites of response were primary tumour (15 patients), cervical nodes (six), mediastinal nodes (four) and pleura (two). Nine of the seventeen responded in more than one site. The median survival times for complete, partial and non-responders were respectively 9.5, 5.6 and 5.2 months.

Response was associated with an improvement in ECOG score in six patients and no change in ECOG score in eight (Table 2). Seven of eight patients with progressive disease showed a deterioration in performance status. Symptoms improved in nine responders and remained the same

Accepted 7 January 1986.
Reprint requests to: Andrew W. Hutcheon, MD Ward 3, Woodend General Hospital, Aberdeen AB9 2YS, U.K.

Table 1. *Response and survival*

	Response category				
	Complete response (C.R.)	Partial response (P.R.)	No change (N.C.)	Progression (P.)	Totals
Stage					
Limited	6 (50%)	2 (17%)	1	3	12
Extensive	2 (12%)	7 (41%)	3	5	17
Histological type					
Squamous	5 (26%)	6 (32%)	3	5	19
Large cell	0	2	0	2	4
Adenocarcinoma	3	1	1	1	6
Survival (mos)					
Range	4–18	1–10	1–12		
Median	9.5	5.6	5.2		

Table 2. *Response and quality of life*

	Response category				
	C.R.	P.R.	N.C.	P.	Totals
ECOG score					
Better	3	3	0	0	6
Same	4	4	3	1	12
Worse	1	2	1	7	11
Symptom score					
Better	4	5	0	0	9
Same	2	3	3	1	9
Worse	2	1	1	7	11

Table 3. *Toxicity*

Toxic effect	Number of patients with toxic effect (%)
Nausea	15 (52%)
Alopecia	11 (38%)
Malaise	8 (28%)
Neurotoxicity	5 (17%)
Anaemia	3 (10%)
*Leucopenia	2 (7%)
Vomiting	2 (7%)
Skin rash	1 (3%)
†Thrombocytopenia	1 (3%)
* WCC nadir (cells/mm^2)	
≥ 4000	21
3000–3999	6
2000–2999	1
1000–1999	1
† Platelet count nadir (cells/mm^3)	
≥ 150,000	21
100,000–149,000	7
≤ 100,000	1

in five. No improvement was observed in non-responders.

In general the treatment was well tolerated although six patients stopped treatment because of side-effects (Table 3). In the remainder, myelosuppression was not a problem and although half the patients became nauseated during treatment, the incidence of vomiting was only 7%. Eight patients complained of troublesome lethargy and malaise during treatment. There was one unexpected death in a man (with a complete response) who suffered relentless clinical deterioration associated with fever and dyspnoea but no obvious infection.

DISCUSSION

The study showed that this combination is active in the treatment of inoperable NSCLC. Activity was particularly marked in patients with adenocarcinoma, who had a 50% complete response rate. Treatment was generally well tolerated with a particularly low incidence of vomiting and myelosuppression. Although the numbers were small, these data suggest that this combination may be as effective as vindesine and *cis*-platinum in NSCLC but less toxic, and we feel that this merits further investigation.

Acknowledgements — We would like to thank Dr. Marie Bakowski, Medical Adviser to Eli Lilly and Co. Ltd., for her helpful comments regarding the manuscript.

REFERENCES

1. Bakowski MT, Crouch JC. Chemotherapy of non-small cell lung cancer: a reappraisal and a look to the future. *Cancer Treat Rev* 1983, **10**, 159–172.
2. Gralla RJ, Caspar ES, Kelsen DP, *et al.* Cisplatin and vindesine combination chemotherapy for advanced carcinoma of the lung: a randomized trial investigating two dosage schedules. *Ann Intern Med* 1981, **45**, 414–420.
3. Lanzotti VS, Thomas DR, Boyle LE, *et al.* Survival with inoperable lung cancer. *Cancer* 1977, **39**, 303–313.
4. World Health Organization. *Handbook for Reporting Results of Cancer Treatment.* WHO Offset Publ No. 48 Geneva, WHO, 1979.