Eur J Cancer Clin Oncol, Vol. 22, No. 12, pp. 1539–1540, 1986.
Printed in Great Britain

0277-5379/86$3.00+0.00

Letter to the Editor

CDDP and 5-FU after Prior VBM or VBM after Prior CDDP and 5-FU in the Management of Recurrent Squamous Cell Carcinoma of the Head and Neck?

A. GRIMALDI, M. MERLANO, G. GARDIN and R. ROSSO
Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy

IT'S LONG been suggested that responses to further chemotherapy are more difficult to obtain after a patient's tumor becomes resistant to the first antineoplastic drug regimen administered. Certain drugs more than others seem to produce this phenomenon that has been observed after radiotherapy as well and it has been suggested that agents with known mutagenic effects may induce the emergence of drug resistant clones with a much higher frequency than the natural spontaneous mutation rate [1]. This consideration may have important clinical implications mainly in the palliative treatment of advanced disease. For example, a drug able to increase the natural mutation rate toward a certain resistant phenotype, should be employed after the use of less mutagenic drugs and thus the possibility of response to further chemotherapy may be higher. In this connection, we present herein a retrospective analysis of two groups of patients with relapsing squamous cell carcinoma of the head and neck.

The characteristics of the two series are reported in Table 1, with the main difference being the sequence of drug administration. The first group consisted of 14 patients (group A) in which a methotrexate based regimen followed prior treatments including surgery radiation and chemotherapy (CDDP + 5-FU). The treatment consisted of: Vinblastine 6 mg/m^2, hour 0, Bleomycin 30 U hour 6, methotrexate 200 mg hour 24, leucovorin rescue 45 mg hour 48.

No objective response was observed and disease progressed in all patients after 1–4 courses. The regimen was dropped. The second group (group B) consisted of 11 patients in which cisplatin-containing chemotherapy was given after radiation, surgery and chemotherapy (methotrexate, Vinblastine, Bleomycin).

Table 1. Characteristics of patients

	I series	II series
Male/female	13/1	9/2
Median age (range)	58 (33–75)	56 (45–74)
Median PS ECOG scale (range)	1 (0–2)	1 (1–3)
Sites of relapse:		
Oropharynx	3	3
Oral cavity	2	2
Hypopharynx	1	1
Maxillary sinus	2	–
Rhinopharynx	–	2
Soft tissue	4	1
Nodes	4	5
Previous treatment:		
S → RT → CT	4	3
S + RT + CT	1	1
S → RT + CT	4	3
S + RT → CT	2	2
RT → CT	2	1
CT + RT → S	–	1
S → CT	1	–
Patients responding to prior chemotherapy	10/14	6/11

S: surgery; RT: radiotherapy; CT: chemotherapy.

The cisplatin based treatment was as follows: CDDP 20 mg/m^2 in 2 hr hydration and 5-FU 200 mg/m^2 push, [2], daily per 5 consecutive days every third week. Four patients reached an objective response. This value compared to the 0% of the previous described series, was analyzed according to the Fisher test [3] for the small number and the difference was statistically significant ($P < 0.03$). Although difficult to demonstrate even in experimental systems, the possibility that the

Accepted 5 June 1986.
Correspondence and reprints requests to: Marco Merlano, Division of Medical Oncology, Istituto Nazionale per la Ricerca sul Cancro, V. le Benedetto XV 10, 16133, Genova, Italy

CDDP-5-FU regimen facilitates the occurence of resistance to VBM (VLB + BLM + MTX) regimen emerges as a significant clinical observation. More importantly, our study indicates that this phenomenon may be prevented if the CDDP-5-FU combination is given after VBM has failed.

REFERENCES

1. Mulkins MA, Heidelberger C. Isolation of Fluoropyrimidine resistant murine leukemie cell lines by one step mutation and selection. *Cancer Res* 1982, **42,** 956–964.
2. Merlano M, Tatarek R, Grimaldi A, Margarino G, Rosso R. Phase I-II with Cisplatin and 5-FU in recurrent head and neck cancer: an effective outpatient schedule. *Cancer Treat Rep* 1985, **69,** 961–964.
3. Armitage P. *Statistical Methods in Medical Research.* Blackwell Scientific Publications, 1971, 138.