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Letters

A Phase I/II Study on Hyperfractionated Chemoradiation Using Chemotherapy as Part of Each Fraction of Treatment in Locally Far Advanced Head and Neck Cancer

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USING CHEMOTHERAPY as a part of each fraction of treatment in concurrent chemoradiation is theoretically most attractive, but feasibility studies on this approach are lacking at present. Based on a hyperfractionated schedule of irradiation developed by EORTC [1] and the documented interaction between irradiation and carboplatin in experimental systems [2–4] we have performed a phase I/II study aimed at investigating whether a dose of carboplatin could be added to each fraction of treatment using the irradiation schedule mentioned. Each fraction consisted of the administration of 5 mg/m^2 carboplation + 115 cGy; two fractions a day were administered 5 days a week up to a total dose of 350 mg/m^2 carboplatin + 8050 cGy to the primary tumours and neck masses.

From February 1993 to February 1995, 30 unresectable head and neck cancers (2 stage III and 28 stage IV) were treated (Table 1). All patients completed their treatments and 24 of them (80%) did it exactly as planned. No otic, renal or neurotoxicity were observed, mucositis remained within the level expected with irradiation alone and 4 cases of occasional nausea or vomiting were seen. One severe (less than 1000 WBC/ml), 5 moderate (WBC between 2000 and 3000) and 2 mild (WBC between 3000 and 4000) leucopenia were observed. One severe (less than 10 000/ml) and 5 moderate (more than 60 000 /ml) thrombocytopenia were also observed. Four transfusions were needed.

Ninety-three per cent (28/30) achieved complete responses (CR) and 7% (2/30) achieved partial responses for an overall response rate of 100%. 3 local recurrences, 1 death due to intercurrent disease and 6 distant metastases without local recurrence were observed. 18 patients are free of disease at a maximum follow-up of 24 months (mean 14.5). Actuarial disease-free survival and local control are 55% and 80%, respectively.

*Table 1. Description of the treated diseases**

Site	Number of patients	Stage III	Stage IV
Floor of the mouth	2	—	2
Pyriform sinus	9	1	8
Nasopharynx	1	1	—
Tonsil	6	—	6
Soft palate	1	—	1
Base of the tongue	6	—	6
Mobile tongue	1	—	1
Paranasal sinuses	1	—	1
Unknown	3	—	3
Total	30	2	28

*23 patients presented fixed nodes, 7 patients bilateral nodes, 10 patients multiple nodes, 14 patients nodes greater than 3 cm, and 12 patients nodes greater than 6 cm.

These data show that our schedule is clinically feasible and very active. The high rate of CR obtained makes the short-term results of this schedule encouraging, particularly considering the high proportion of unfavourable subsites and far-advanced diseases treated. The rate of CR obtained with current irradiation schedules in such advanced diseases is normally lower than that of this study. We consider that the addition of chemotherapy to each fraction of treatment probably contributed to the killing of a greater proportion of tumour cells that would have been killed by radiation alone.

While past and present protocols of concurrent chemoradiation in head and neck cancer commonly intercalate the administration of drugs or combinations within a course of irradition [5–7], presumably the maximum degree of interac-

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tion occurs when chemotherapeutic drugs are present at any time irradiation is administered. Giving chemotherapy as part of each fraction of treatment is one of the best sequences by which this can be reached. Our study is one example of a way of approaching the combination of irradiation and chemotherapy.

In conclusion, our schedule is feasible and represents an uncommon but encouraging way of facing the treatment of advanced head and neck cancer.

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