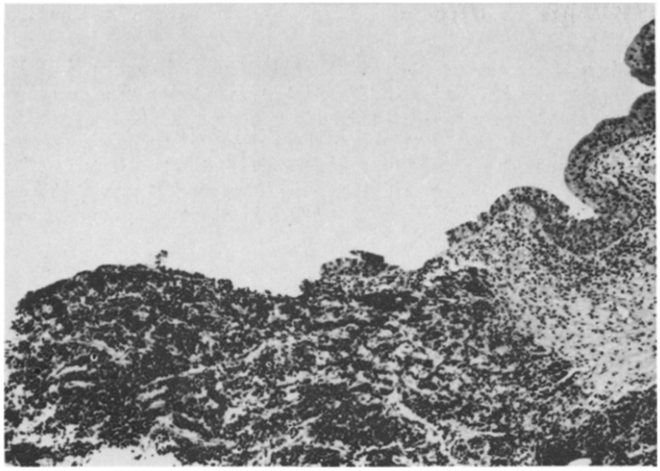

Fig. 1. SCC of the bladder showing solid sheets of small cells with hyperchromatic nuclei and scanty cytoplasm. (haemotoxylin/eosin 10 ×).

line is at present the most probable [4], suggested by the frequent finding of other carcinomas with SCC. The diagnosis of neuroendocrine carcinoma of the bladder poses several problems: a vesical metastasis has to be excluded and such lesions have to be differentiated from transitional cell carcinoma, lymphoma, paraganglioma and peripheral nerve neuroblastoma.

The incidence of these tumours will probably tend to increase because of the increasing use of immunohistochemical techniques. Since extrapulmonary SCC are rare, standard therapeutic approaches have not been developed, but several treatments have been proposed. Surgery, more or less conservative, and radiotherapy are the preferred treatments, as used in transitional cell carcinoma of the bladder. The usefulness of combining chemotherapy with conventional radiotherapy and surgery has been suggested [5–7]. Interpretation of the prognosis of bladder SCC is limited by the small number of well documented cases, but the high malignancy of this neoplasm is demonstrated by the frequent metastatic diffusion of the disease in a short time. Our case confirms the aggressiveness of this tumour.

1. Yu DS, Chang SY, Wang J, *et al.* Small cell carcinoma of the urinary tract. *Br J Urol* 1990, **66**, 590–595.
2. Davis, BH, Ludwig ME, Cole SR, Pastuszak WT. Small cell neuroendocrine carcinoma of the urinary bladder: Report of three cases with ultrastructural analysis. *Ultrastruct Pathol* 1983, **4**, 197–204.
3. Cramer SF, Aikawa M, Cebelin M. Neurosecretory granules in small cell invasive carcinoma of the urinary bladder. *Cancer* 1981, **47**, 724–730.
4. Ibrahim NB, Briggs, JC, Corbishley CM. Extrapulmonary oat cell carcinoma. *Cancer* 1984, **54**, 1645–1661.
5. Podesta AH, True LD. Small cell carcinoma of the bladder. Report of five cases with immunohistochemistry and review of the literature with evaluation of prognosis according to stage. *Cancer* 1989, **64**, 710–714.
6. Blomjous CEM, Vos W, De Voogt HJ, Van der Valk P, Meijer CJLM. Small cell neuroendocrine carcinoma of the urinary bladder. A clinicopathologic, morphometric, immunohistochemical and ultrastructural study of 18 cases. *Cancer* 1989, **64**, 1347–1357.
7. Oosterling JE, Brendler CB, Burgers JK, Marshall FF, Epstein JI. Advanced small cell carcinoma of the bladder. Successful treatment with combined radical cystoprostatectomy and adjuvant methotrexate, vinblastine, doxorubicin and cisplatin chemotherapy. *Cancer* 1990, **65**, 1928–1936.

Eur J Cancer, Vol. 28A, No. 4/5, pp. 1005–1006, 1992.
Printed in Great Britain
0964–1947/92 $5.00 + 0.00

Severe Complications of 5-Fluorouracil and Cisplatin with Concomitant Radiotherapy in Inoperable Non-metastatic Squamous Cell Oesophageal Cancer After Intubation—Early Termination of a Prospective Randomised Trial

A.S. Alberts, W. Burger, F. Greeff, L. Schoeman, D. Friediger, J. Nel, E. Steyn, E.U. Schmid and G. Falkson

In a recent review [1] of 1926 cases of oesophageal cancer in South Africa, it was shown that 77.4% of all cases had stage III AJC disease. Palliative intubation was the treatment most often selected. The median survival of patients with advanced oesophageal cancer in South Africa is 3–4 months[2, 3]. Despite the advanced stage of disease some patients will present with good performance status and are potential candidates for more intensive anticancer therapy. Seitz *et al.* [4] demonstrated considerable activity with concomitant 5-fluorouracil (5-FU) and cisplatin in patients with oesophageal cancer. In the present trial the addition of radiotherapy to concomitant 5-FU and cisplatin (postintubation) was therefore prospectively evaluated.

20 patients with advanced, inoperable squamous carcinoma of the esophagus and ECOG [5] performance status of 0, 1 or 2, were entered on study. Pretreatment staging was done with barium swallow, computed tomography, and endoscopy. All patients had had placement of either a Celestin or Procter–Livingstone tube and could swallow semi-solid food and maintain adequate nutrition afterwards. Patients with tracheobronchial bulging due to tumour or small mediastinal fistulae were admitted to the study provided that the area was well covered by the tube and no frank tracheo-bronchial fistulae were present (Table 1).

Patients had to have adequate renal, haematologic and hepatic function. After intubation eligible patients were randomised to no further treatment (observation) or radiotherapy and concomitant 5-FU and cisplatin. Radiation therapy consisted of 4 Gy fractions daily from day 1–5 (20 Gy) and 29–33 (20 Gy). A 3-field technique was used with the fields covering at least 5 cm superior and inferior, and 2 cm lateral to the known tumour volume. The chemotherapy consisted of 5-FU 600 mg/m^2 over 24 h from days 1–5 and 29–33 and cisplatin 15 mg/m^2 daily from days 1–5 and 29–33.

Correspondence to A.S. Alberts.
A.S.Alberts, D. Friediger and J. Nel are at the Department of Radiotherapy, University of Pretoria, P.O. Box 667, Pretoria, 0001 South Africa; W. Burger, L.Schoeman and G. Falkson are at the Department of Medical Oncology, and F. Greeff, E. Steyn and E.U.Schmid are at the Department of Surgery, University of Pretoria, Pretoria, South Africa.
Revised 16 Sep. 1991; accepted 2 Dec. 1991

Table 1. Patients' characteristics

Characteristic	Treatment groups: Tube only	Tube + chemotherapy + radiotherapy
No. of patients (total 20)	10	10
Male : female	10 : 0	9 : 1
Median age (years)	53	55
Performance status (ECOG)		
1	5	5
2	5	5
Differentiation of tumour		
Well	—	2
Moderate	10	8
Location of primary tumour		
Upper thoracic	1	—
Middle thoracic	9	6
Lower thoracic	—	4
Tracheo-bronchial involvement or small mediastinal fistulae	4	4
Median length of tumour (cm)	7	8
Median survival (weeks)	19	11

An interim analysis showed that patients randomised to observation had a median survival of 19 weeks while patients treated with radiotherapy, 5-FU and cisplatin had a median survival of 11 weeks, ($P = 0.03$, Mantel–Cox test). This difference in survival was due to toxicity of the combined chemoradiotherapy and tube. This made early termination of the trial ethically necessary.

The documented haematological toxicity of the 10 patients on the chemoradiotherapy arm was mild to moderate (ECOG grade I–II) in 3 patients and severe (ECOG grade III) in 1 patient. Gastrointestinal toxicity was acceptable with mild to moderate nausea and vomiting in 4 patients (ECOG grade I–II). 3 patients developed pulmonary infection requiring antibiotic treatment. 2 patients developed ECOG grade III neuromotor complications which fully reversed.

A lethal perforation of the oesophagus developed in 1 patient outside the tumour area, shown at postmortem to be related to oesophagitis and mechanical stress of the tube. In this patient 80% tumour necrosis was also demonstrated with multiple representative sections of the tumour at necropsy. 3 patients on chemoradiotherapy died at home after 25, 25 and 36 days, with a clinical picture related to toxicity, and not progressive disease. Confirmation with necropsy could not be obtained as the patients lived in rural areas.

The chemoradiotherapy combination has considerable reported tumour activity [4]. It should, however, not be used (at least in Southern Africa) for patients with far advanced disease where intubation has been selected for palliation. The 4 deaths due to complications occurred despite the selection of cytostatic doses in the lower range as the radiation dose was high per fraction. Whether the combination of 5-FU and cisplatin plus radiotherapy will prolong survival of patients with advanced disease still needs to be confirmed in a prospective randomised trial. We are currently randomising patients after dilatation to observation vs. chemoradiotherapy. Furthermore, patients with mediastinal fistulae or involvement of tracheo-bronchial tree are now excluded.

1. Mannell A, Murray W. Esophageal cancer in South Africa. A review of 1926 cases. *Cancer* 1989, **64**, 2604–2608.
2. Alberts AS,Anderson JD, Goedhals L, Cronje JDE,Doman MJ. Pallierende bestraling skedules met en sonder chemoterapie in gevorderde karsinoom van die esofagus. (Palliating radiation schedules with and without chemotherapy in advanced carcinoma of the esophagus). *S Afr Med J* 1984, **66**, 289–291.
3. Walker ARP, Walker BF, Isaacson C, Segal I, Pryor S. Short duration of survival among South African Blacks with oesophageal cancer. *S Afr Med J* 1984, **66**, 877–878.
4. Seitz JF, Giovannini M, Padaut-Cesana J, *et al.* Inoperable non-metastatic squamous cell carcinoma of the esophagus managed by concomitant chemotherapy (5-fluorouracil and cisplatin) and radiation therapy. *Cancer* 1990, **66**, 214–219.
5. Oken M, Creech RH, Tormey DC, *et al.* Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am Clin Oncol* 1982, 5, 649–655.

Acknowledgement—Supported in part by a grant from the Medical Research Council (A.S.A., D.F., J.N.) and the National Cancer Association of South Africa (W.B., L.S., G.F.).

Eur J Cancer, Vol. 28A, No. 4/5, pp. 1006–1007, 1992.
Printed in Great Britain
0964–1947/92 $5.00 + 0.00

Palliation of Malignant Phaeochromocytoma with Combination Chemotherapy

Suresh Senan, Nicholas Reed and John Connell

RECENT REPORTS have highlighted the role of ^{131}I-labelled meta-iodobenzylguanidine (MIBG) in the diagnosis and treatment of malignant (metastatic) phaeochromocytoma and have dismissed any useful role for chemotherapy [1, 2]. However, only 60% of our patients with malignant phaeochromocytoma show MIBG uptake. This may be due to tumour dedifferentiation and occurs in cases initially showing uptake [2]. Here, we describe useful symptomatic and biochemical responses in 2 patients with this tumour whose lesions did not show MIBG uptake.

Patient 1, a 17-year-old-female, presented in September 1988 with palpitations and chest pain. She was hypertensive, had elevated plasma noradrenaline (radioenzymatic assay [3]) and a left extra-adrenal tumour with multiple bony metastases. Biopsy of a rib lesion revealed metastatic phaeochromocytoma and an ^{131}I MIBG scan showed no uptake. The hypertension was controlled with atenolol and phenoxybenzamine and a left-sided extra-adrenal tumour was excised in November 1988. Three postoperative noradrenaline levels remained high (61–113 nmol/l) and she started chemotherapy every 3 weeks with cyclophosphamide 750 mg/m^2 on day 1, vincristine 1.4 mg/m^2 day 1 and dacarbazine 600 mg/m^2 on days 1 and 2, receiving seven cycles of chemotherapy between December 1988 and April 1989.

Correspondence to Suresh Senan.
S. Senan and N. Reed are at the Beatson Oncology Centre, Western Infirmary, Glasgow G11 6NT, U.K. and J. Connell is at the MRC Blood Pressure Unit, Western Infirmary.
Revised 5 Dec. 1991; accepted 6 Dec. 1991.