



Fig. 1. Electron micrographs: A = large round endocrine granules with fine wavy limiting membrane, $\times 20\,000$; inset shows cross-cut profile of microfilaments (F) (up to 15 nm in diameter, $\times 22\,000$). B = neoplastic cell showing irregularly developed microvilli on the luminal surface, numerous endocrine granules and a pool of microfilamentous structures, $\times 7800$. C = endocrine granules showing somatostatin (gold staining), $\times 13\,350$.

The tumour of our case is undoubtedly a member of the carcinoid family [7], and one of primitive-gut endocrinomas [8]. Demonstration by peroxidase staining of somatostatin in many neoplastic cells, and calcitonin only in a few cells, led us to the diagnosis of carcinoid somatostatinoma.

1. Ganda OP, Weir GC, Soeldner JS, *et al.* "Somatostatinoma": A somatostatin-containing tumor of the endocrine pancreas. *N Engl J Med* 1977, **296**, 963–967.
2. Kovacs K, Horvath E, Ezrin C, Sepp H, Elkan I. Immunoreactive somatostatin in pancreatic islet-cell carcinoma accompanied by ectopic ACTH syndrome. *Lancet* 1977, **i**, 1365–1366.
3. Larsson LI, Hirsch MA, Holst JJ, *et al.* Pancreatic somatostatinoma: Clinical features and physical implications. *Lancet* 1977, **i**, 667–668.
4. Soga J, Tazawa K. Pathologic analysis of carcinoids: Histologic reevaluation of 62 cases. *Cancer* 1971, **28**, 990–998.
5. Weichert RF III, Reed R, Creech O JR. Carcinoid-islet cell tumors of the duodenum. *Ann Surg* 1967, **165**, 660–699.
6. Dayal Y, Tallberg KA, Nunnenmacher G, De Lellis RA, Wolfe HJ. Duodenal carcinoids in patients with and without neurofibromatosis. A comparative study. *Am J Surg Pathol* 1986, **10**, 348–357.
7. Soga J. So-called apudoma and gastrointestinal carcinoid (urgut endocrinoma). *J Clin Sci* 1977, **13**, 1362–1369 (Japanese).
8. Soga, J. Carcinoids: Their changing concept and a new histological classification. In: Fujita T, ed. *Gastro-Entero-Pancreatic System—A Cell Biological Approach*, Gustav Fischer Verlag, 1973, 101–119.

Eur J Cancer, Vol. 26, No. 10, pp. 1108–1109, 1990.
Printed in Great Britain
0277-5379/90 \$3.00 + 0.00
Pergamon Press plc

Phase II Study of Carboplatin in Untreated Inoperable Advanced Stomach Cancer

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CISPLATIN, one of the most active agents in stomach cancer, has limited application because of toxicity [1]. Carboplatin has shown some activity in stomach cancer [2, 3] and causes less nephrotoxicity, vomiting and ototoxicity than cisplatin [4]. We did a non-randomised phase II study of carboplatin, given on days 1, 3 and 5 every 4 weeks, as the antineoplastic activity of carboplatin is schedule-dependent in animals [5, 6].

Patients with inoperable, metastatic, histologically confirmed stomach cancer with measurable lesions were enrolled. Eligibility requirements included: age less than or equal to 70 years, life expectancy greater than or equal to 3 months, WHO status less than or equal to 2, no brain metastases, no previous chemotherapy or radiotherapy, adequate bone marrow, renal and liver functions, and normal serum electrolytes and audiogram. All patients gave informed consent. Neoplastic lesions were measured before each cycle and 4 weeks after the last cycle. Complete haemogram, serum creatinine and creatinine clearance, electrolytes and liver function were similarly monitored. During chemotherapy, complete blood counts were done twice weekly.

Chemotherapy consisted of 130 mg/m² carboplatin on days 1, 3 and 5 by intravenous infusion over 30 minutes without hydration. After the first course, dose modifications were planned to adjust drug doses to individual patients. If the nadirs of leucocytes and platelets were between 1500–2500/ μ l and 75 000–100 000/ μ l, respectively, full treatment was administered. If the lowest leucocyte and platelet count was greater than 2500/ μ l and 100 000/ μ l, respectively, the dose of carboplatin was increased to 160 mg/m². If the nadirs of leucocytes and platelets were less than 1500/ μ l and 75 000/ μ l, respectively, carboplatin was given at a dose of 100 mg/m². Cycles were to be repeated every 4 weeks if white blood cells and platelets were greater than 4000/ μ l and 100 000/ μ l, respectively, or delayed until these values were achieved. Low-dose anti-emetics were prophylactically administered. Patients with progressive disease after the

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Table 1. Carboplatin toxicities at starting dose level (A) and at 160 mg/m² (B)

	1		2		3	
	A	B	A	B	A	B
Leukopenia	6	1	5	5	0	1
Thrombocytopenia	3	2	2	5	2	0
Anaemia	7	2	2	1	0	1
Nausea/vomiting	9	5	2	0	0	0
Diarrhoea	0	0	1	0	0	0
Alopecia	5	1	0	0	0	0
Infections	0	0	1	0	0	0

A = starting dose: 23 patients, 48 cycles (median 2, range 1–4).

B = dose level 160 mg/m²: 11 patients, 20 cycles (median 2, range 1–4).

first cycle or without major response after the third cycle received salvage treatment with ELF [7]. Patients were considered evaluable for response and toxicity if they had received at least one cycle of carboplatin. Tumour response, response duration and toxicity were classified according to WHO criteria [8].

24 consecutive patients were studied: 20 men, 4 women, age range 49–77 (median 65), WHO status 0–2 (median 1). 23 were evaluable for response and toxicity. Chemotherapy was discontinued for 1 patient after the first dose of carboplatin due to empyema of the gall bladder. 23 patients received 68 cycles of carboplatin (median 3, range 1–6) and 11 received 20 courses at 160 mg/m². Carboplatin induced 2 (9%) partial remissions with a duration of 4 months each (95% CI 0–21%). 13 patients (57%) showed no change and 8 (35%) had progressive disease. 20 patients received salvage treatment with ELF. One CR and 9 PR for an overall response rate of 50% were achieved.

The worst toxicities are outlined in Table 1. Leucopenia and thrombocytopenia (grade 3) were observed in 0 and 7% of the patients at starting dose level, and in 9 and 0% of the patients after dose escalation to 160 mg/m² intravenously on days 1, 3 and 5, respectively. Anaemia (grade 3) occurred in 1 patient who was treated at the higher dose level. The median nadir of leucocytes and platelets was observed on days 14 and 16, respectively. Median time to recovery for leucocytes and thrombocytes was 20 and 21 days, respectively after start of cycles. Non-haematological toxicities above grade 2 were not seen.

We have confirmed the good tolerance of carboplatin. The main haematological side-effect was thrombocytopenia which was severe in 7%. The remission rate in our study (9%) was low, and is similar to response rates reported in other studies [2, 3, 9]. Overall, studies show that carboplatin induced 4 partial responses in 67 patients (6%, 95% CI 0–21%). These data suggest that carboplatin has marginal activity in the tested schedules in stomach cancer.

4. Rozenzweig M, Martin A, Beltangady M, *et al.* Randomized trials of carboplatin versus cisplatin in advanced ovarian cancer. In: Bunn PA, Canetta R, Ozols RF, Rozenzweig M, eds. Carboplatin (JM-8): Current Perspectives and Future Directions. Philadelphia, Saunders 1990, 175–186.
5. Furiiazis, AP, Yagoda A, Kyriazis AA, Fogh J. Response of nude mouse-grown human urothelial cancer to cis-diamminedichloroplatinum (II), diammine (1,1-cyclobutane-dicarboxylato)platinum (II) and mitoguazone dihydrochloride. *Cancer Res* 1985, 45, 2012–2018.
6. Kyriazis AP, Kyriazis AA, Yagoda A, Fogh J. Response of nude mouse-grown adenocarcinomas of the human exocrine pancreas to cis-diamminedichloroplatinum (II), diammine (1,1-cyclobutane-dicarboxylato(2-)-0,0'-platinum) and mitoguazone dihydrochloride. *Cancer Res* 1985, 45, 4354–4359.
7. Stahl M, Wilke H, Preusser P, *et al.* Etoposide (E), leukovorin (L), 5-FU (F) (ELF) in advanced gastric carcinoma (GC)—final results of a phase-II-study, *Proc ECCO* 1989, 5, Abstr. P-0695.
8. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer* 1981, 47, 207–214.
9. Kim DJ, Kim NK, Meng KH, *et al.* Phase II trial of carboplatin (CBDCA) in patients with advanced adenocarcinoma of the stomach [abstract 442]. *Proc ASCO* 1989, 8, 114.

Eur J Cancer, Vol. 26, No. 10, pp. 1109–1110, 1990.
Printed in Great Britain
0277-5379/90 \$3.00 + 0.00
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Untunnelled Subclavian Vein Catheters in Haemato-oncology Patients

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IN HAEMATO-ONCOLOGY, reliable venous access through indwelling right atrial catheters is necessary in an increasing number of patients. Unlike tunnelled Hickman-like catheters and subcutaneous ports of the Port-A-Cath type, untunnelled catheters can be inserted, removed and reinserted simply [1–3]. We report our prospective study of untunnelled subclavian vein catheters in 200 patients over a 19-month period.

The “short-term” group ($n = 48$) included patients who required a catheter only for administration of high-dose and/or continuously infused chemotherapy. Patients who were pancytopenic for longer than 7 days and who were candidates for intensive care were included in the “long-term” group ($n = 152$), and received partial, intestinal decontamination with colistin, trimethoprim and amphotericin [4]. Febrile patients were evaluated by physical examination, chest X-ray, blood cultures and other investigations as indicated. If granulocytopenic, patients received broad-spectrum intravenous antibiotics, using

1. Preusser P, Achterath W, Wilke H, *et al.* Chemotherapy of gastric cancer. *Cancer Treat Rev* 1988, 15, 257–277.
2. Einzig A, Kelsen DP, Cheng E, *et al.* Phase II trial of carboplatin in patients with adenocarcinomas of the upper gastrointestinal tract. *Cancer Treat Rep* 1985, 69, 1453–1454.
3. Beer M, Cavalli F, Kaye SB, *et al.* A phase II study of carboplatin in advanced or metastatic stomach cancer. *Eur J Cancer Clin Oncol* 1987, 23, 1565–1567.

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