the double helix, DNA and biotechnology and DNA and oncology. For further information contact D.A. Chambers, Department of Biochemistry, Center for Molecular Biology of Oral Diseases, The University of Illinois at Chicago, A-312 College of Medicine West (M/C 536), 1853 West Polk Street, Chicago, Illinois 60612, U.S.A.

Clinical Trials in Oncology

A conference on clinical trials in oncology: improving their design and analysis will be held on 28–30 October 1993 in Toronto, Ontario, Canada. For further information contact Continuing Medical Education, University of Toronto, Medical Sciences Building, Toronto, Ontario M5S 1A8, Canada. Tel: (416) 978-2719, Fax: (416) 971-2200.

Innovative Cancer Chemotherapy

The XI Chemotherapy Foundation symposium on innovative cancer chemotherapy for tomorrow will be held on 10–12 November 1993 in New York City, U.S.A. Topics covered will include phase I-II cancer agents, chemoprevention, gene therapy and new diagnostic and prognostic procedures. For further information contact J. Silverman, Division of Medical Oncology, Box 1178, Mount Sinai School of Medicine, One Gustave Levy Place, New York, NY 10029, U.S.A. Tel: (212) 241 6772, Fax: (212) 996 5787.

European Society for Medical Oncology

The XIX ESMO congress will be held on 19–22 November 1994 in Lisbon, Portugal. For further information contact Secretariat ESMO, Via Sadine 22, 6900 Lugano, Switzerland. Tel: (41) 91 57 54 11, Fax: (41) 91 57 57 44.

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Letters

Epirubicin, Etoposide and Cisplatin in Advanced Pancreatic Carcinoma

Maria Di Bartolomeo, M. Giulia Zampino, Angelo Di Leo and Emilio Bajetta

MOST PATIENTS with pancreatic cancers present with locally advanced or metastatic disease. The disease is suitable for curative resection in only 10% of patients, who have a 5-year survival rate of 6% [1]. In the presence of unresectable tumour, the prognosis following medical treatment is poor, and median survival ranges from 3 to 5 months. Furthermore, studies carried out using both single and multiple chemotherapeutic agents have been characterised by a low response rate, short response duration and only occasional complete remissions [2, 3].

In view of the encouraging results obtained with the association of etopside (VP16), doxorubicin and cisplatin (CDDP) in the treatment of gastric cancer, this combination was used to treat patients with advanced pancreatic cancer [4, 5].

Eligible patients had histologically documented pancreatic adenocarcinoma with measurable lesions. Other inclusion criteria were age $\leq$ 65 years, an ECOG performance status of 0–2, adequate kidney, cardiac and hepatic function, and normal bone marrow reserve (leucocyte count $\geq$ 4000/mm^3, platelet count $\geq$ 100 000/mm^3). The exclusion criteria were previous medical treatment or an expected survival of $<$ 2 months. Informed consent was obtained in all patients in accordance with institutional regulations.

Treatment consisted of epirubicin 40 mg/m^2 intravenously (i.v.), a 50-min infusion of VP16 120 mg/m^2 i.v., and a 30-min infusion of CDDP 40 mg/m^2 i.v. Each drug was administered on days 1 and 8, and the cycle was repeated every 3 weeks. Cisplatin infusion was begun immediately after the administration of epirubicin and VP16 and was preceded and followed by a 2-h i.v. infusion of 500 ml of 5% dextrose and 500 ml of saline solution. Toxicity and response were evaluated according to WHO/UICC criteria [6]. Treatment was delayed for 1 week in the presence of leucocyte and platelet counts $\leq$ 4000 and 100 000/mm^3, respectively. If grade 3 toxicity persisted, the doses were further reduced by 25%; treatment was stopped in the case of grade 4 toxicity. A maximum of six cycles was planned.

Complete blood counts were made weekly, and biochemistry profiles were drawn up before each course. Chest and skeletal X-ray, ultrasound and computed tomography scans were performed to define the measurable lesions before the start of treatment, and subsequently every two cycles in order to evaluate response.

Time to progression was calculated from the start of treatment to the clinical and/or radiological documentation of progressive disease.

10 patients (4 males and 6 females) with locally advanced (4 patients) or metastatic pancreatic carcinoma (6 patients) were treated; all were evaluated for toxicity and response. The median age was 55 (range 45–61), ECOG performance status was 0 for 4 patients and 1 for 6 patients. In 8 patients disease was monitored in the pancreas, 6 in liver metastases and 1 in the adrenal. A total of 37 courses was administered, with a median of three cycles per patient (range 2–6). No objective responses were observed; 4 patients had stable and 6 had progressive disease. Median time to progression was 3 months (range 2–9). Dose reductions due to myelosuppression were required in 35% of the cycles, and 60% were administered after a 1-week delay. Grade 4 leukopenia and neutropenia were detected in, respectively, 1 and 5 patients. Infectious episodes were reported in 2 cases, whereas no treatment-related deaths were observed. Grade 3 stomatitis occurred in 3 patients. Nausea and vomiting were uncommon.

Pancreatic adenocarcinoma remains resistant to chemotherapy. Despite the many conventional drugs tested, no remarkable response rate or positive impact on survival has been observed [7, 8]. Several trials have been conducted to investigate

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whether a multi-drug regimen containing fluorouracil (FU) is more effective than FU alone. Cullinan *et al.* have recently investigated polychemotherapy in a randomised study but failed to demonstrate any significant improvement in survival [9].

Our study shows that epirubicin, VP16 and CDDP combination is ineffective in inducing objective responses in patients with advanced pancreatic carcinoma.

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Phase II Trial of Iproplatin in Advanced Squamous Cell Carcinoma of the Head and Neck, Oesophagus and Lung

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IPROPLATIN (CHIP), a cisplatin analogue, shows moderate activity in cisplatin-responsive tumours—advanced ovarian and urothelial cancer, brain tumours and squamous carcinomas of the uterine cervix, lung [1, 2] and head and neck [3, 4]. However, optimal dosages and schedules have not yet been determined.

In a multicentre phase II trial, 82 patients [male, advanced squamous cell carcinoma, free of previous chemotherapy, performance status (WHO) ≤ 2] were treated at doses of 75 mg/m^2/day, for 4 or 5 consecutive days, every 4 weeks.

The response rate in head and neck carcinoma was 20% (95% confidence limits 9–21), with one complete response and nine partial responses. But for oesophagus or lung carcinoma, the response rates were 0 and 11% (0–26%). The probability of response was dose-independent and higher for previously unirradiated sites (21 vs. 8%, $P = 0{,}28$).

Major toxicity was haematological, especially for platelets as in previous studies [5, 6] and iproplatin had some gastrointestinal toxicity (grade 2 or 3 for 28 and 10% of patients, respectively). 1 patient died with myeloaplasia and renal insufficiency. No serious hypersensitivity reactions were observed.

At this dose and schedule, iproplatin appears to have a very low efficacy for squamous cell cancer of head and neck, oesophagus or lung in our trial and the same toxicity as carboplatin.

Table 1. Haematological toxicity

		Maximum nadir level across all cycles (WHO grades)				
		0	1	2	3	4
Initial dose (mg/m^2)						
300	WBC	16	2	9	2	0
	PL	13	4	3	6	3
375	WBC	18	10	5	8	2
	PL	16	4	11	11	7

Nadir white blood cell: χ^2 (trend) = 1.156 on 1 degree of freedom, $P = 0.282$. Nadir platelet: χ^2 (trend) = 1.310 on 1 degree of freedom, $P = 0.252$.

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