Table 1. Toxicity

	WHO grade					
	0	1	2	3	4	NK
White cell nadir						
90 mg/m²*	0	0	3	3	0	2
100 mg/m²*	0	0	1	0	0	0
110 mg/m²*	0	0	0	7	3	2
All doses†	0	0	3	11	5	2
Platelets						
90 mg/m²*	6	0	0	0	0	2
100 mg/m²*	1	0	0	0	0	0
110 mg/m²*	8	0	1	1	0	2
All doses†	17	0	1	1	0	2
Nausea and vomiting†	1	5	6	8	0	1
Alopecia†	2	3	5	10	0	1
Stomatitis†	12	6	1	1	0	1

*First course.
†Worst course.
NK = not known.

No patients had an objective response. 1 patient had a subjective response with improvement in performance status. 3 patients did not progress on treatment (no change response category) but 2 of them progressed within 6 weeks of completing chemotherapy. The median duration of survival was 5 months (range 1–11) and 16 (76%) patients have died. There were no treatment-related deaths.

Toxicity is summarized in Table 1. The dose-limiting toxicity was neutropenia with a nadir white cell count below 2.0×10^9/l in all patients treated with 110 mg/m² of epirubicin. In view of this and the lack of response higher doses of epirubicin were not tested. The treatment caused significant alopecia in 15 patients despite scalp cooling. Nausea and vomiting were troublesome in 14 patients despite prophylactic anti-emetics.

Epirubicin had at best minimal activity in platinum-resistant ovarian cancer. Despite increasing the dose to the maximum tolerated dose, there were no objective responses. Bone marrow suppression was the dose-limiting toxicity and was often severe, leading to dose reductions. Subjective toxicity was significant with nausea, vomiting, anorexia and alopecia all detracting from the quality of life.

Alternative approaches to the treatment of relapsed ovarian cancer are urgently needed but it seems unlikely that any of the currently available cytotoxic agents will be of benefit. Patients with platinum-resistant ovarian cancer are therefore an ideal group for the testing of new drugs. There is no indication for the use of epirubicin, even at high doses, in ovarian cancer patients after exposure to a platinum compound.

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Unresponsiveness of Pancreatic Adenocarcinoma to Antioestrogen Therapy

W. Scheithauer, G. Kornek, K. Haider and D. Depisch

A NEW APPROACH to the treatment of advanced pancreatic carcinoma was suggested in 1981 with the demonstration of sex hormone receptors in these tumours [1]. Confirmation of this finding in human and in experimentally induced murine tumours [2, 3], as well as demonstration of the inhibiting effect of hormonal manipulation on the growth of human pancreatic adenocarcinoma xenografts in nude mice [4], stimulated clinical evaluation. Encouraging preliminary results were observed in small uncontrolled studies, mainly with tamoxifen [5–7]. Since some phase III trials were started but not reported, we decided to re-evaluate this therapeutic concept.

26 consecutive patients with pathologically confirmed advanced adenocarcinoma of the pancreas that was not potentially curable by surgery entered the study between May 1988, and August 1989 (Table 1). 19 patients had a laparotomy for biopsy, palliative bypass procedures, or partial pancreatectomy and 7 patients had the diagnosis established by ultrasound-guided needle biopsy without laparotomy. Previous treatment had to be completed at least 6 weeks before entry. Informed consent was obtained in all patients.

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Table 1. Patients' characteristics

	No. of patients
M/F	10/16*
Median age (yr)	62 (35–87)
Median Karnofsky performance status (%)	70 (40–90)
Measurable or assessable disease	19
Sites of involvement	
Single	7
Multiple	19
Liver	15
Previous treatment	
Palliative bypass surgery	16
Chemotherapy	6†
5-FU/radiotherapy	3

*4 premenopausal, 12 postmenopausal.
†5-fluorouracil (5FU) alone or in combination.

With confirmation of tissue diagnosis and known unresectable tumour as documented by laparotomy or radiological investigation, treatment was started with tamoxifen 20 mg orally twice daily. Patients were followed up every 2–3 months until death. Although desirable, measurable or assessable disease was not required in this trial. The endpoint of evaluation was survival from time of diagnosis. Oestrogen receptor status was not assessed in the pancreatic tumour specimens.

Among the 19 patients with assessable or measurable disease, none had objective tumour response. All patients have died at the time of analysis. Survival did not vary significantly by sex. Median survival for women and men was 4.6 and 4.1 months, respectively. The median survival for the entire group of 26 patients was 4.4 months. There was no toxicity associated with tamoxifen administration.

The lack of objective tumour response in the patients with evaluable disease and the median overall survival were similar to the natural history of untreated metastatic pancreatic cancer. Those results were not only disappointing, but also contrasted with the results of other studies that used the same dose and schedule of tamoxifen [5, 6]. In addition we found no survival benefit for postmenopausal patients as described by Wong *et al.* [7].

In a small study there is the risk of accruing, by design or chance, a skewed population that may have a preponderance of good or poor prognostic factors. Several adverse prognostic factors in our patients, such as poor performance status and a high proportion with liver metastases, might have influenced our results. However, apart from the few other negative reports on the efficacy of tamoxifen in pancreatic cancer [8], the outcome of controlled studies started in Stockholm, Norway and the U.K. in mid-1987 [9], has not been reported. Hormonal treatment of advanced pancreatic cancer might appear attractive due to the ineffectiveness of conventional chemotherapy, the excellent tolerance and low costs of oral anti-oestrogens, and the encouraging preliminary clinical studies. However, we believe that such treatment cannot be recommended unless its effectiveness is proven convincingly in prospective randomized trials. Hormonal manipulation with certain other drugs such as high-dose megestrol acetate, aimed at producing subjective improvement and at increasing appetite and weight [10], could be considered in pancreatic cancer.

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Cancer Cells in Effusions and Increases in T-Activated Lymphocytes

Massimo Geuna, Alessandra Linari and Gianni Bussolati

EFFUSIONS CONTAINING cancer cells model immune reactivity to cancer since, reflecting the tumour and host immune relations, they may represent what is occurring in solid tumours. 49 effusions from patients with or without cancer were investigated with markers of lymphocyte subsets and activation.

Effusions arriving at our laboratory for cytological examination were selected when the cell count was over 3–5 × 10^5/ml. 24 effusions contained cancer cells (breast 12, lung 6, ovary 4, bladder 1, and pancreatic 1). 5 other patients had cancer but their effusions were free of cancer cells. 20 cases were reactive effusions from patients with either cirrhosis or pleuritis. 1 patient had B chronic lymphocytic leukaemia. Cancer cells were identified cytologically and by staining with HMFG2 antibody and immunoperoxidase [1, 2]. 1–5 × 10^5 cells were tested with monoclonal antibodies [3] against T cells and subsets (Leu

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