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An EORTC Gastrointestinal Group Phase II Evaluation of Epirubicin Combined with 5-Fluorouracil in Advanced Adenocarcinoma of the Pancreas

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Abstract—*The EORTC Gastrointestinal Group has conducted a phase II trial in 47 patients with locally advanced or metastatic adenocarcinoma of the pancreas with epirubicin 90 mg/m² intravenously on day 1 in combination with 5-fluorouracil 500 mg/m² in a 2 hr infusion day 1–4, every 4 weeks. Of 43 evaluable patients there were six early deaths due to tumour progression and one due to a cerebrovascular accident. There were six partial responses for a response rate of 14% including early deaths. The median survival for all patients was 4 months. It is concluded that the addition of 5-fluorouracil to epirubicin does not appear to enhance the therapeutic results of epirubicin alone.*

INTRODUCTION

PROGNOSIS in advanced adenocarcinoma of the pancreas is dismal [1]. Only few single agents have activity in this disease and 5-fluorouracil (5-FU) has been the most extensively evaluated drug [1]. Epirubicin has been studied by the EORTC Gastrointestinal (GI) Group and yielded a response in eight (22%) of 38 patients including early deaths due to tumour progression [2]. Because data from the literature suggest that the response rate from 5-FU might be around 20% the EORTC GI Group decided to evaluate the combination of epirubicin and 5-FU in patients with measurable locally advanced or metastatic adenocarcinoma of the pancreas.

MATERIALS AND METHODS

Patients with histologically proven measurable adenocarcinoma of the pancreas were entered in the trial. Eligibility, response and risk criteria have been previously described [2]. Epirubicin was given in a dose of 90 mg/m² intravenously (i.v.) on day 1 in combination with 5-FU, 500 mg/m² in a 2 hr infusion, day 1–4, every 4 weeks. Response was evaluated after every two cycles.

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Table 1. Patient characteristics

Evaluable patients	43
Median age (years)	59
Male/female	29/14
Median Zubrod scale	1
Median weight loss (percentage of previous body weight)	1–5%
Locally advanced	12
Locally advanced + metastatic	29
Metastatic (primary excised)	2

RESULTS

From January 1984 to March 1986 47 patients from 12 institutions out of five countries were registered. Three patients were not eligible, two had no pancreatic cancer and one was pretreated. One patient was considered not evaluable because of insufficient treatment (refusal after one course). The patient characteristics are shown in Table 1. Of these 43 patients there were six early deaths due to tumour progression and one early death due to a cerebrovascular accident. These cases are considered failures. There were six partial remissions

Table 2. Results

Number of evaluable patients	43
Early death due to tumour progression	6
Early death due to other reason	1
Partial remission	6
No change	14
Progressive disease	16
Median duration of response (months)	7
Median survial all patients (months)	4

for a response rate of 14% (95% confidence interval 4–24%). The median duration of response was 7 months (range 2–9 months). Fourteen patients experienced stable disease for at least 2 months. The median survival for all eligible patients was 4 months. These results are summarized in Table 2.

The median number of administered cycles was 3 (range 1–8). Toxicity of the treatment was mild and consisted of hair loss, median grade 2 and nausea/vomiting, median grade 1. Mucositis grade 1 or 2 occurred in 14%. The median white cell count on day 14 was 2.4 × 10^9/l (range 0.9–6.7). There were no toxic deaths.

DISCUSSION

Epirubicin has been tested by the EORTC Gastrointestinal Group and yielded a response rate of 22% [2]. These results have been confirmed by others [3]. Although the two consecutive phase II trials cannot be compared the combination of 5-FU with epirubicin, with a response rate of 14%, does not appear to offer an advantage over epirubicin or 5-FU alone.

REFERENCES

1. Macdonald JS, Gunderson LL, Cohn I. Cancer of the pancreas. In: De Vita V, Hellman S, Rosenberg SA, eds. *Cancer. Principles and Practice of Oncology*. Philadelphia, Lippincott, 1982, 563–589.
2. Wils J, Bleiberg H, Blijham G *et al.* Phase II study of epirubicin in advanced adenocarcinoma of the pancreas. *Eur J Cancer Clin Oncol* 1985, **21**, 191–194.
3. Hochster H, Green MD, Speyer JL, Wernz JC, Blum RH, Muggia FM. Activity of epirubicin in pancreatic carcinoma. *Cancer Treat Rep* 1986, **70**, 299–300.