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Clinical Trials Summaries

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

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INTRODUCTION

CHEMOTHERAPY still has a limited role in the treatment of advanced pancreatic cancer and no measurable impact on the expected median survival of 4–5 months. Epirubicin without or with 5-fluorouracil (5-FU) has subsequently been studied by the EORTC Gastrointestinal (GI) Group and yielded response rates of 22 and 14% respectively [1, 2]. Based on data from the literature suggesting that ifosfamide has activitiy in pancreatic cancer [3, 4], we decided to evaluate the combination of epirubicin and ifosfamide in this disease.

MATERIALS AND METHODS

Patients with histologically or cytologically proven measurable locally advanced or metastatic adenocarcinoma of the pancreas were entered in the trial. Eligibility and response criteria have been previously described [1]. Epirubicin was administered in a dose of 90 mg/m^2 intravenously (i.v.) on day 1 in combination with ifosfamide, 5 g/m^2 in a 24 h infusion, day 1, every 4 weeks. Mesna was given in a dose of 500 mg, i.v., every 8 h for four doses.

RESULTS

From August 1986 till November 1987, 32 patients were registered. The patient characteristics are depicted in Table 1. Of 32 patients there were nine early deaths or early progressions. Four patients (12.5%; 95% confidence interval: 4–30%) had a partial response, documented by CT scan. The durations of these responses were 3, 6, 8 and 13 months. The median survival of all patients was 5 months (Table 2).

The median number of administered cycles was two (range 1–8). The toxicity was severe with 43% of patients experiencing WHO grade 4 leucopenia, 21% grade 3–4 thrombocytopenia and 23% grade 3–4 nausea/vomiting. Because of the hematological toxicity, dose reduction or postponement of treatment was necessary in 50% of patients who received at least two cycles.

DISCUSSION

The lack of significant activity of epirubicin and ifosfamide observed with this particular schedule

Table 1. Patient characteristics

Eligible patients	32
Median age (range)	59 years (38–69)
Male/female	18/14
Median Zubrod scale (range)	1 (0–2)
Median weight loss (percentage of healthy body weight)	1–10%
Locally advanced	11
Locally advanced + metastatic	18
Metastatic, primary excised	2
Locoregionally recurrent	1

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Table 2. Results

Number of patients	32
Early death/early progression	9
Partial remission	4
No change	11
Progressive disease	8
Median duration of response (months)	7
Median survival all patients (months)	5

may partly be explained by the toxicity, leading to frequent dose reductions as prescribed in the protocol (25% dose reduction in case of grade 4 nadir leucopenia). It is possible that ifosfamide has a better therapeutic index when administered in a 3–5 day continuous infusion [5]. Two more recent studies, however, concluded that ifosfamide lacks significant activity in pancreatic cancer. In one trial, one partial remission of 29 patients and in the second one complete and one partial response of 30 patients were reported [6, 7].

The response rate of this study falls within the confidence limits of our previous studies and fails to support the superiority of combination chemotherapy over single agents.

Chemotherapy of pancreatic carcinoma remains a major oncologic challenge. There is no standard treatment and patients should only be treated in clinical trials.

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