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Clinical Trial Summary

A Phase II Study of a 21 Day Continuous Infusion Schedule with Epirubicin in Advanced Gastric Cancer

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INTRODUCTION

One of the most active analogs of doxorubicin is epirubicin. It has exhibited less cardiac toxicity and equal or higher antitumor activity [1]. In several phase II studies, patients with advanced gastric cancer were treated with epirubicin in different doses, leading to response rates of 0–27% [2]. Based on a phase I study with continuous infusion of epirubicin during 21 days [3], we started a phase II study to evaluate the efficacy and toxicity of a continuous infusion with epirubicin in a dose of 6 mg/m^2/day during 21 days in patients with advanced metastatic gastric cancer.

PATIENTS AND METHODS

Criteria for entry were: progressive, histologically proven, measurable metastatic gastric carcinoma; age 18–75 years; normal renal and bone marrow function (creatinine <130 μmol/l, leukocytes >3000/mm^3, platelets >100,000/mm^3, serum bilirubin <35 mmol/l); Karnofsky performance score >60; and normal cardiac function including normal ECG and no history of overt cardiac disease defined as cardiac angina or cardiac decompensation.

Epirubicin was given in a continuous infusion schedule over 21 days in a dose of 6 mg/m^2/day. Courses were repeated every 6 weeks if no unacceptable toxicity (grade III/IV according to the WHO criteria) [4] occurred and no progression of tumor growth was recorded. The drug was administered via a totally implantable venous access port (Infuse-A-Port®) and a portable syringe driver (Graseby Medical MS 16A®) as reported earlier [5].

The hospital pharmacy prepared sterile, plastic wrapped syringes (Monoject®), each with the correct amount of epirubicin, dissolved in 10 ml sterile water, for 24 h infusion.

RESULTS

In 29 patients a total of 82 cycles were administered. Three patients were not evaluable for response. Two complete responses (36+, 13 months), two partial responses (21 and 36 weeks), and one minor response were observed in the evaluable patients. Seventeen patients had stable disease with a median duration of 13 weeks (range 6–36). Treatment was well tolerated and toxicity was limited. One patient developed the hand-foot syndrome. WHO grade 3 leukocytopenia was seen in four patients, grade 1 transient nausea and transient vomiting in respectively five and two patients, moderate and complete hairloss in respectively seven and six patients, and four patients experienced WHO grade 2 and one grade 3 mucositis. Two patients developed a subclavian vein thrombosis, which was correlated to the presence of the venous access port catheter.

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Table 1. Patient characteristics and results

	No. of patients
Entered in the study	29
Age in years:	
mean 54.5	
range 38–69	
Male/female	25/4
Site of metastases/disease (more than one site possible):	
retroperitoneal and abdominal lymph node	19
liver	9
supraclavicular lymph nodes	1
lung	1
carcinomatous peritonitis	1
ovaries	1
bone	1
Prior therapy:	
surgical resection of the primary tumor	6
chemotherapy (MTX/5-FU)	4
chemotherapy (MOPP) for a non-Hodgkin's lymphoma 10 years earlier	1
Number of cycles administered to the 26 evaluable patients (a total of 80)	
1 cycle	2
2 cycles	8
3 cycles	6
4 cycles	5
5 cycles	2
6 cycles	1
8 cycles	1
Response:	
complete remission	2
partial remission	2
minor response	1
stable disease (6–36 weeks)	17
progressive disease	4

CONCLUSION

Continuous infusion of epirubicin does result in responses in patients with advanced gastric cancer. Compared to bolus administration, this infusion schedule shows less toxicity, but additional morbidity might be caused by the implantable venous access port used for drug administration.

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