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Short report

High-dose epirubicin in chemotherapy refractory non-seminomatous germ cell cancer: A phase II study

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Summary. Eighteen patients with progressive disseminated, platinum-resistant germ cell tumors were treated with epirubicin 135 mg/m^2, every 3 weeks. One patient had stable disease, 17 developed progression. Myelosuppression was dose-limiting. One patient died of neutropenic septicemia. High-dose epirubicin is not active against platinum-resistant germ cell cancer.

Key words: epirubicin, germ cell cancer, testicular cancer

Introduction

Presently, the cure rate of metastatic germ cell tumors is in the order of 85% as a result of induction chemotherapy with cisplatin, etoposide and bleomycin [1, 2]. The probability of cure mainly depends on the extent of disease and the serum concentrations of tumor markers [3]. The results of salvage chemotherapy are generally poor and rather a function of response duration and extent of disease at the time of relapse than choice of drugs and treatment strategies [4]. Hence, the search for new drugs continues. In 1987, epirubicin 90–135 mg/m^2, every 3 weeks, was reported to be effective in patients with cisplatin resistant germ cell tumors [5]. Therefore, we performed a phase II trial of epirubicin 135 mg/m^2, every 3 weeks, in such patients.

Patients and methods

Patients were eligible if they had histologically proven, measurable, progressive non-seminomatous germ cell cancer, which was clearly resistant to cisplatin chemotherapy. Other requirements were a performance status WHO scale 0–2, a life expectancy of at least 2 months, WBC $\geq 3 \times 10^9$/l, platelets $\geq 100 \times 10^9$/l and normal renal and excretory liver function.

Epirubicin was given at a dose of 135 mg/m^2 i.v bolus, every 3 weeks. If WBC and platelets had not fully recovered, therapy was postponed for a maximum of 2 weeks. In these cases epirubicin was resumed at a dose of 110 mg/m^2. A similar dose reduction was required if WBC nadir was $<0.5 \times 10^9$/l, or platelets $<20 \times 10^9$/l in the absence of symptoms, or WBC $0.5–1.0 \times 10^9$/l with fever, or platelets $20–50 \times 10^9$/l with bleeding. Two cycles of therapy were required to enable assessment of response, unless there was early progressive disease. Response and toxicity were evaluated according to WHO criteria.

Results

Eighteen eligible and evaluable patients were entered. Patient characteristics are presented in Table 1. Fifteen patients had testicular non-seminomas, and 3 had extragonadal tumors. Seven patients had previously been treated with one platinum containing chemotherapy regimen, 6 with 2, 3 with 3 and 2 with 4.

Table 1. Patient characteristics.

No. of patients entered	18
Age (years): median	27
range	18–46
Performance (WHO): median	1
range	0–2
Prior radiotherapy	8
Prior chemotherapy	
Number of regimens: median	2
range	1–5
Number of drugs: median	5
range	3–7
Interval since end of prior chemotherapy:	
median (weeks)	12
range	2–45

Three patients received one cycle of epirubicin, 11 had 2, 2 had 3, and 2 had 4 cycles. Hematologic toxicity could be evaluated in 15 patients. Leukocytopenia grade 3–4 occurred in 12 patients (80%), and thrombocytopenia grade 3–4 (27%). One patient died of neutropenic septicemia.

Non-hematologic toxicity comprised nausea and vomiting grade 2–3 in most patients. Cardiotoxicity and severe mucositis were not observed.

Treatment with epirubicin failed in 17 patients who developed progressive disease, including 3 early progressions and one toxic death, whereas one patient with tumor markers only had no change for a duration of 10 weeks.

Discussion

This study failed to show activity of high-dose epirubicin in extensively pretreated patients with platinum refractory germ cell tumors. This outcome is in keeping with the results reported by Harstrick et al. [6] who observed one partial response in 15 heavily pretreated patients, who were treated with epirubicin 100–120 mg/m^2, every 3 weeks. When we combine the available data, 4 of 53 patients (8%) have responded [5, 6]. It can be concluded that high-dose epirubicin is inactive against platinum resistant germ cell cancer.

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