Eur J Cancer Clin Oncol, Vol. 25, No. 6, pp. 995–996, 1989.
Printed in Great Britain

0277-5379/89$3.00 + 0.00
© 1989 Pergamon Press plc

Clinical Trials Summaries

Phase II Trial of Esorubicin in Advanced Renal Carcinoma

P. HURTELOUP, P. CHOLLET, H. ROCHE, B. CHEVALLIER, P. CAPPELAERE, M. VAN GLABBEKE, M. HAYAT and J.P. ARMAND for the Clinical Screening Group of the EORTC

INTRODUCTION

ESORUBICIN (4′-deoxydoxorubicin) is an analog of doxorubicin in which the 4′-hydroxyl group has been removed. Pre-clinical studies showed that esorubicin has a similar or even higher activity compared to doxorubicin and produces lower cardiotoxicity than doxorubicin when both are used at equitherapeutic doses [1–3]. The phase I trials conducted with esorubicin recommended a starting dose of 35 mg/m^2 [4, 5]. Leucopenia was the dose-limiting toxicity. This study was undertaken by the EORTC Clinical Screening Group to test the efficacy of esorubicin in patients with renal carcinoma.

PATIENTS AND METHODS

To be eligible for entry into this study, all the patients had to have a histologically proven renal carcinoma, a progressive and measurable disease surgically uncurable, a Performance Status (ECOG–WHO scale) <3, an age <70 and adequate hematologic (WBC >4000/mm^3, platelets >120,000/mm^3), renal (creatininemia <130 μmol/l), and hepatic (bilirubicin <35 μmol/l) functions. No prior palliative chemotherapy was allowed. A normal cardiac history and function were mandatory. Informed consent was requested according to institutional rules.

Esorubicin was supplied by Farmitalia Carlo Erba in vials containing 5 or 10 mg of 4′-deoxydoxorubicin as a lyophilized hydrochloride salt. Patients were treated with a starting dose of 35 mg/

Table 1. *Characteristics of eligible patients*

Characteristics	No. of patients
Patients	21
Sex	
Male	16
Female	5
Age	
Median	70
Range	30–71
Performance status	
WHO: 0	4
WHO: 1	8
WHO: 2	9
Prior radiotherapy	6
Prior chemotherapy	2
Site of disease	
Lung	16
Primary	10
Liver	8
Soft tissue	7
Esorubicin administration	
No. of cycles	
Median	3
Range	2–11
Side-effects (no hematological)	
Nausea/vomiting	10
Alopecia	9
Venous irritation	2
Diarrhea	2
Response	
Complete	1
Partial	1
No change	9
Progression	10

Accepted 25 January 1989.
Participating institutions
Hôpital Universitaire St Pierre, Brussels; Centre Claudius Regaud, Toulouse; Institut Jean Godinot, Reims; Institut Gustave Roussy, Villejuif; Centre René Gauducheau, Nantes; Centre G.F. Leclerc, Dijon; Centre Jean Perrin, Clermont-Ferrand; Centre Oscar Lambret, Lille; Centre Henri Becquerel, Rouen; Institut Curie, Paris; Centre A. Vautrin, Vandoeuvre-les-Nancy; Centre René Huguenin, Saint-Cloud; Centre Eugène Marquis, Rennes; C.M.C. Foch, Suresnes; Fondation Bergonié, Bordeaux and EORTC Data Center, Brussels.
Reprint requests to: P.Hurteloup, Clinical Screening Group EORTC, Département d'Oncologie, Radiothérapie, Hôpital Jean Minjoz, CHR Besançon Blvd Flemming, F-25030 Besançon, France.

m^2 every 3 weeks. Retreatment was postponed by 1 week if a full hematologic recovery was not obtained on day 21 and the doses adjusted according to the degree of myelosuppression.

The drug was first diluted in a solution of 5% dextrose in water; but, due to local venous reactions, the drug was subsequently administered in a normal saline solution and given by rapid i.v. infusion.

Therapeutic activity was assessed according to the WHO criteria after a minimum of two treatment cycles [6].

RESULTS

Out of the 21 eligible patients (pts) entered in the trial, 19 were considered as evaluable for response. The reasons for not being evaluable were early death (1 pt) and concomitant corticosteroid (1 pt).

The population studied consisted mainly of non-pretreated patients (only 5 patients had been previously irradiated). Seven of those 19 patients had a performance status equal to 2.

Two objective responses (1 complete and 1 partial response) were reported. These two untreated patients had measurable lung metastases. The durations of responses were 22 and 113+ weeks respectively.

The median cumulative dose of esorubicin administered was of 105 mg/m^2 ranging from 35 to 350 mg/m^2.

Esorubicin was well tolerated; the drug induced moderate (WHO grade 1–2) nausea/vomiting and alopecia. One severe venous reaction, resulting in treatment discontinuation, was reported, and a typical anthracycline myelosuppression was observed (median nadir value recorded during the first cycle WBC = 2150/mm^3, range 1000–3700/mm^3; median nadir value observed throughout all cycles: WBC = 1800/mm^3, range 1000–3700/mm^2). No cardiac side-effect was noted.

DISCUSSION

Despite the fact that a long lasting complete response has been reported, we have to conclude that the activity of esorubicin in advanced renal carcinoma was minimal under the conditions of our study.

REFERENCES

1. Arcamone F, Penco S, Redaelli S, Hanessian S. Synthesis and antitumor activity of 4′-deoxydoxorubicin and 4′-deoxyadriamycin. *J Med Chem* 1976, **19**, 1424–1425.
2. Casazza AM. Experimental evaluation of anthracycline analogs. *Cancer Treat Rep* 1979, **63**, 835–844.
3. Casazza AM. Antitumor activity and cardiac toxicity of 4′-deoxydoxorubicin in mice. In: Mathé G, Maral R, Dejager R, eds. *Anthracyclines. Current Status and Future Developments.* New York, Masson, 1980, 193–197.
4. Guiliani FC, Zirvi KA, Kaplan NO *et al.* Chemotherapy of human colorectal tumor xenografts in athymic mice with clinically active drugs: 5-fluorouracil and BCNU. Comparison with doxorubicin derivatives 4′-deoxydoxorubicin and 4′-*O*-methyl-doxorubicin. *Int J Cancer* 1981, **27**, 5–13.
5. Rozencweig M, Crespeigne N, Kenis Y. Phase I trial with 4′-deoxydoxorubicin (esorubicin). *Invest New Drugs* 1983, **1**, 309–313.
6. Miller AB, Hoogstraten E, Staquet M *et al.* Reporting results of cancer treatment. *Cancer* 1981, **47**, 207–214.