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Negative Phase II Study with Carboplatin and 5-Fluorouracil in Advanced Breast Cancer

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THOSE PATIENTS with advanced breast cancer progressing to first-line chemotherapy have a poor prognosis and there is no accepted second-line standard treatment [1]. Since cisplatin has significant activity against metastatic breast carcinoma, we decided to explore the activity of its analogue, carboplatin, plus 5-fluorouracil (5-FU) in these patients.

Selection criteria included: diagnosis of advanced breast cancer failing at least one regimen that included anthracyclines, presence of evaluable or measurable disease, life expectancy of 12 weeks or more, Karnofsky index 60% or higher, age 70 or under, no previous exposure to cisplatin or its analogues, no chemotherapy or radiotherapy within 4 weeks before treatment, leucocytes 3500/ μ l, and serum creatinine and bilirubin both 1.2 mg/dl or less. Patients gave signed informed consent.

Carboplatin 60 mg/m² on days 1–5 was administered as a 30 min infusion; and 5-FU, 1 g/m² per day was delivered in continuous infusion over 120 h. The schedule was repeated every 4 weeks. In the absence of progressive disease, patients had to receive at least two cycles of treatment to be considered evaluable for activity. WHO criteria were used for response and toxicity.

From October 1986 to December 1990, 21 patients were entered. 1 patient was not evaluable because of inadequate therapy, and one other due to protocol violation. The characteristics of the 19 evaluable patients are presented in Table 1. All patients had received 5-FU before. There was 1 partial response, 5 patients had stable disease, and 13 progressed, for an overall activity of 5% (95% confidence interval 7.5–30.0%). The partial remission occurred in a patient with liver metastases and lasted 8 weeks. The median time to progression was 2 months (range 1–9). 1 patient is still on treatment with stable disease. Toxicity (grade 2 or more) was: leucocytes (6 patients), platelets (4), nausea/vomiting (7), stomatitis (7), diarrhoea (3) and alopecia (1).

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Table 1. Patients' characteristics

Sex (M/F)	1/18
Median age (range)	59 (38–70)
Karnofsky index	70 (50–80)
Predominant Sites	
Soft tissues	4
Bone	3
Viscera (liver)	12 (4)
Measurable Disease	12
Evaluable disease	7
Previous chemotherapy	
First line	12
Second line	7
Third line	1

Thus carboplatin plus 5-FU had minimal activity as second-line therapy in patients with advanced breast cancer progressing after regimens which included anthracyclines and 5-FU. Our data are consistent with two previous negative reports for carboplatin in this setting [2, 3]. The 120-h continuous infusion of 5-FU we used did not appear to influence the results, in contrast to the significant activity showed by protracted infusions of 5-FU, which had an objective response rate of 30–32% in previously treated patients with metastatic breast carcinoma [4, 5]. Carboplatin has been tested in metastatic breast cancer in phase II trials as first-line therapy with moderate activity as a single agent. [6, 7].

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