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Clinical Trials Summaries

A Phase II Study of Carboplatin in Advanced or Metastatic Stomach Cancer*

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Cisplatin was shown to have some activity in gastric cancer [1–6]. This drug has also been used in a few combination chemotherapy trials [7–9].

The different toxicity pattern of carboplatin prompted the study group to evaluate the antitumor activity of this cisplatin analog in gastric cancer [10, 11].

PATIENTS AND METHODS

Fifty-three patients with histologically confirmed, advanced or inoperable adenocarcinoma of gastric origin participated in the trial between January 1984 and March 1986. Measurable or evaluable disease, age ≤ 75, a performance status of 1–3 (WHO), life expectancy of 8 weeks, serum creatinine 120 μmol/l, WBC 4×10^9/l, platelet counts 100×10^9/l were required. Treatment had to be started after a period of 4 weeks after the last course of prior chemotherapy. Blood counts were assessed weekly, blood chemistry before every course and tumor size every two courses. Tumor response and toxicity were rated according to World Health Organization recommendations. Two full courses of treatment were required prior to response assessment, except in case of early, rapid progression; patients with progressive disease were taken off the study.

Protocol treatment consisted of carboplatin, 400 mg/m^2 infused i.v. in 150–250 ml dextrose 5%, once every 5 weeks. The dose per course was reduced to 350 mg/m^2 for the last 8 patients with prior treatment, after cases of toxic death were reported.

RESULTS AND DISCUSSION

The characteristics of the patients are shown in Table 1. Three patients had received a second chemotherapy which in one, contained cisplatin.

Exposure to carboplatin and toxicity are shown in Table 2. A drop in hemoglobin levels by 1–5 g/dl was seen in 16 patients. Six of the patients with an elevated serum creatinine (120–160 μmol/l) recovered to normal during treatment, while one patient died of bleeding with a creatinine of 250 μmol/l. The following on-treatment conditions were also recorded: facial dysesthesia, pulmonary thromboembolism, fever, cerebral ischemic accident and diarrhea. Three deaths were attributable to toxicity, of sepsis in one patient previously treated with FAM, and of bleeding in two others pretreated with fluorouracil, doxorubicin and cisplatin.

Tumor response is reported in Table 3. The term 'early progression' refers to documented disease progression before the end of the first course. Of the three previously untreated patients who received less than the protocol dose, two had 'no

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Table 1. Characteristics of the patients

Entered		53		
No evaluable tumor	4			
Concomitant radiation	1			
Performance status 4	1			
Eligible		47		
27 male, 20 female				
Age				
31–69, median	56			
Performance status (WHO)				
0: 7, 1 (median): 18, 2: 17, 3: 5				
Previous treatment				
Radical surgery:		17		
(Time from surgery 2–55 months, median 21)				
			Previous response	*n* evaluable
Combination chemotherapy:*		27		
FAM	21		3	12
AF	3		0	3
FAP	2		2	2
Disease localization				
Primary/abdominal wall recurrence	22			
Liver	21			
Nodes	13			
Bone	3			
Lung	4			
Soft tissue/skin	3			
Ascites/pleural fluid	9			

*F: fluorouracil, A: doxorubicin, M: mitomycin, P: cisplatin.

Table 2. Carboplatin treatment

1–9 courses, median 2.	Dose per course	193–460 mg/m² (median 400)
Total courses 47	Total dose	240–3300 mg/m² (median 800)
(1 course only: 21 patients)		

Toxicity	(Fully documented: 33 patients)	
Hematologic	Pretreated (21)	Non-pretreated (12)
Platelets (× 10^9/l)		
Nadir range 10–310, day 15–35 (median 22)		
100	5	7
50–100	8	3
25–50	3	2
25	5	0
WBC (× 10^9/l)		
Nadir range 0.7–10.8, day 11–42 (median 27)		
4.0	6	7
2–4	9	4
1–2	2	1
1	3	0

Non-hematologic	(43 patients assessed)	
	WHO grade	Number
Nausea/vomiting	1	11
	2	18
	3	3
Renal	1	7
Hair loss	2	6
Stomatitis	1	1
	2	1
Paresthesia	1	1

Table 3. Response evaluation

Previously treated patients		
Eligible		27
Response not evaluable:		7
Treatment stopped too early	2	
Follow-up stopped too early	1	
Combination treatment	1	
Toxic death	3	
Response evaluable:		20
Partial response	2	(2, 4+ months)
No change	1	(3 months)
Progression	17	
(Early progression: 6)		
Previously untreated patients		
Eligible		20
Response not evaluable		5
Early death, tumoral	4	
Early death, PTE	1	
Response evaluable		15
Partial response	1	(12 months)
No change	6	(3–12 months, median 5.5)
Progression	8	
(Early progression: 3)		

change'. Indicator lesions in the responding patients were primary tumor, abdominal wall recurrence, lung and lymph node metastases.

The 95% confidence intervals for the response rate are 0–32% in the non-pretreated group and 0.1–24% in the other. This minimal response rate is compatible with recently published data [12]. The pattern of toxicity is also similar to published results; in particular, the three cases of toxic death stress the necessity of a dose reduction for previously treated patients.

These data confirm also that the inclusion of patients with a poor performance status is likely to impair the evaluability of phase II studies.

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