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A Phase II Study of Cis-Platinum for Recurrent Corpus Cancer*†

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INTRODUCTION

SINCE the introduction of Cis-platinum (DDP) as an active anticancer agent in the mid-seventies, several reports have appeared on the effect of this drug, single or in combination in various kinds of malignancies. From a gynecological point of view the drug has been tested in cases of ovarian and cervical cancer with rather good response rate [1–3]. Little data are available regarding the use of DDP alone in the treatment of recurrent and metastasizing endometrial carcinomas. Loeb *et al.* reported complete responses in two of two patients [4], whereas no response has been observed by Rossof *et al.* [3] in a total of six patients. We felt that a phase II study of DDP in patients with recurrent endometrial carcinomas who had not received prior chemotherapy was warranted.

MATERIALS AND METHODS

Eleven patients with recurrent endometrial carcinomas with the following criteria were accepted into the study: leukocytes $\geqq 2000$ per mm^3, platelets $\geqq 100{,}000$ and a Karnofsky index $\geqq 60$ and measurable disease. Kidney function and oto-neurologic investigations were monitored during the study.

The median age was 64 yr (range 54–72 yr). All patients had previously undergone preoperative intracavitary treatment after which they were subjected to total hysterectomy and bilateral salpingo-oophorectomy. The initial extent according to FIGO stage was I in five patients, II in five, and IV in one. Histologic examination showed high differentiated in two patients, moderate-low differentiated in two, low differentiated in five, and carcinosarcoma in one. Median relapse-free interval after primary treatment was 3 months (range 0–12 months).

Five of the patients had peripheral recurrence, five had both peripheral and central recurrence, and one had central recurrence alone.

Because of renal toxicity when using 100 mg/m^2 DDP, given as i.v. infusion we lowered the dosages to 50 mg/m^2. Patients were hydrated overnight with at least 2 l of 5% dextrose and 0.5N normal saline. After the overnight hydration 50 mg/m^2 of DDP was diluted in 2 l of 5% dextrose, 0.5 N saline and 37.5 g mannitol and given during 8 hr. Supplemental mannitol infusions were utilised as necessary to maintain a urine output of 100 ml/hr during the DDP infusion and for 12 hr thereafter. The treatment was given with 3 weeks interval.

The treatment results were defined as follows: *complete remission* was a total disappearance of all measurable and evaluable lesions for at least 1 month and partial remission as a more than 50% reduction in the largest diameter of measurable tumour and total regression of evaluable but non-measurable lesions. *Stable disease* was less than 50% decrease in the diameter of measurable lesions or no change in non-measurable lesions and the appearance of no new lesions.

RESULTS

Objective response was obtained in four of the 11 patients (1 CR and 3 PRs) (Table 1). Furthermore two patients had stable disease for a median duration of 8+ months. The CR and the three PRs are still responding

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Table 1. Response to DDP therapy

Patient No.	Tumour site at the beginning of DDP	Response*	Duration (months)	
			Remission	Suvival
1	pulm + skeleton	CR	10+	10+
2	pulm + central†	PR	12+	12+
3	pulm	PR	8+	8+
4	pulm + skeleton	PR	6+	6+
5	pulm	SD	9+	9+
6	pulm	SD	7+	7+
7	pulm + central†	PD	—	12
8	pulm	PD	—	5
9	pulm + central†	PD	—	5
10	central†	PD		4
11	generalized	PD		4

*CR = complete remission; PR = partial remission; SD = stable disease; PD = prograssive disease.

†Central = the upper half of the vagina or centrally in the true pelvis above the vault of the vagina after completion of treatment.

after 10+, 12+, 8+ and 6+ months. Five patients did not respond to the DDP treatment. The median survival for non-responders was 5 months. All of the responding patients had a better quality of life during their remissions.

Side effects

No serious side effects were noted with this treatment. One case of slightly impaired hearing and two points with minor allergic reactions were observed and in two patients creatinine clearance was lowered during the treatment.

CONCLUSION

This phase II study shows that DDP can induce remissions in recurrent endometrial carcinoma. The overall response rate was 36% and no serious effects were noted.

In our opinion DDP as a single agent is a promising new drug in patients with metastasizing or recurrent endometrial carcinoma.

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