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Carboquone Combined with Methotrexate and 5-Fluorouracil for Recurrent and Advanced Ovarian Cancer

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OVARIAN CANCER responds initially well to chemotherapy—over 80% to cisplatin-based combinations [1]. However, tumours usually recur and become drug resistant [2]. Carboquone (CQ) is an alkylating agent resembling mitomycin C in structure and mechanism of action [3]. Ovarian cancer has been reported to respond to carboquone-based drug combinations in about 50% of cases [4]. We conducted a study to evaluate the efficacy of CQ in patients with recurrent and/or advanced ovarian cancer, when combined with methotrexate (MTX) and 5-fluorouracil (FU), both drugs with shown effect in ovarian cancer [5, 6]. The doses per treatment course were: CQ 3 mg/m^2 intravenously (i.v.), MTX 150 mg/m^2 i.v. and FU 600 mg/m^2 i.v. Calcium folinate and $NaHCO_3$ were given to prevent side-effects. The treatment courses were repeated every 4 weeks.

A total of 50 patients received at least one treatment course. The mean age of patients was 58.4 years (range 28–75). All 50 patients were evaluable for toxicity. However, 6 patients had a second tumour (a tubal or uterine carcinoma), and 5 patients were given only one treatment. These 11 patients were excluded from the response analysis. The mean number of treatment courses per patient was 4.4 (range 1–16). The responses assessed according to UICC criteria [7] are given in Table 1. Of 39 evaluable patients, only 4 or 10% (95% confidence interval 2.9–24.2%) responded. 36 patients had been given previous cisplatin-based chemotherapy. Of these, one with an adenocarcinoma had a CR and one with an anaplastic tumour had a PR. On the contrary, the previously untreated tumours responded well: of the only three previously untreated patients one with a serous and one with a granulosa cell tumour had a CR.

The therapy was quite well tolerated. Based on the nadir values (on the day 14 of each cycle), 2 patients had WHO grade 3 thrombocytopenia, 3 patients had grade 3 anaemia, 3 patients had grade 3 leucopenia, and 1 had grade 4. In 1 patient, pretreatment day 28 blood specimens revealed grade 3 thrombocytopenia. Blood transfusions were given when indicated. Nausea and vomiting occurred in most patients but responded to standard antimetic therapy.

Even though CQ has a clear effect in the primary treatment of ovarian cancer, the combination of CQ–MTX–FU at the doses used in the current study seems to have only modest activity after previous failed cisplatin-based chemotherapy. However, a trial using a higher dose of CQ may be warranted in the future.

Table 1. The response of ovarian cancer by histology to a combination of carboquone, methotrexate and 5-fluorouracil in 39 evaluable patients

Histological type	*n*	CR + PR	NC	PD
Serous cystadenocarcinoma	20	1	9	10
Mucinous cystadenocarcinoma	3	0	1	2
Endometrioid cystadenocarcinoma	1	0	1	0
Adenocarcinoma	5	1	3	1
Anaplastic carcinoma	3	1	2	0
Granulosa cell tumour	7	1	6	0
Total	39	4 (10%)	22 (56%)	13 (33%)

CR = complete response; PR = partial response; NC = no change; PD = progressive disease.

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