not that robust in that only 22 of the 45 eligible patients actually were able to receive one or more courses of MGBG. 46 patients were entered in the study because in the first 21 patients we noted hints of antitumour activity (i.e. short-lived tumour shrinkage). However, additional patient accrual indicated that the agent has no appreciable antitumour activity in this population of patients with bladder cancer.

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Carboplatin for Advanced Bladder Cancer

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CARBOPLATIN is an analogue of cisplatin that retains the antitumour activity of cisplatin but has a different spectrum of dose-limiting toxicity [1]. In phase I and II studies a low frequency of emesis, ototoxicity, and peripheral neuropathy and no substantial nephrotoxicity have been reported. Reversible myelosuppression was dose-limiting [2]. Carboplatin can be administered to patients with poor renal function without inducing further impairment. Because the drug is mostly excreted unchanged in the urine, dose attenuation is needed in patients with renal dysfunction to prevent excessive myelosuppression [3, 4]. We report a phase II trial of carboplatin in advanced bladder carcinoma.

Table 1. Toxicity

Who scale	No. with nausea/vomiting	No. with myelosuppression
0	8 (29%)	10 (36%)
1	6 (21%)	3 (11%)
2	9 (32%)	10 (36%)
3	5 (18%)	4 (14%)
4	0 (0%)	1

28 consecutive patients with locally advanced and/or metastatic transitional cell carcinoma of the bladder were entered. Eligibility also included age 70 or under, no previous chemotherapy, Eastern Cooperative Oncology Group (ECOG) performance status 2 or below. Previous surgery or radiation was allowable. Patients with liver metastasis were excluded. Informed consent was obtained.

After admission, patients were treated with carboplatin (Laboratories Ferrer, Barcelona) 400 mg/m^2 in 500 ml Dw5 over 1 h intravenously scheduled for a total of six cycles every 28 days. Anti-emetics were not given in the first course; in patients who were sick more than four times metoclopramide was used in subsequent courses. If the granulocyte count was under 1000/μl and/or the platelet count was below 100,000/μl on day 28, the next course was delayed until these values were exceeded. Patients with creatinine clearance between 20 and 40 or below 20 ml/min had the dose reduced to 250 and 150 mg/m^2, respectively. Patients with disease progression or not attaining partial response after three cycles were taken off the study. If possible, patients with locoregional disease only who achieved a partial response received surgical or radiotherapy treatment. We used the double-sampling design [5].

A complete response (CR) was defined as disappearance of all evidence of tumour. A partial response (PR) was a 50% or greater reduction with no progression in any site. Progression was considered new lesions or an increase of more than 25%. The criteria for CR and PR had to be satisfied on at least two consecutive evaluations a month or more apart. All patients who failed to achieve CR or PR were designated as non-responders (NR) including those who died, had reduced therapy because of toxicity or refused to continue. Toxicity was evaluated for all patients [6].

The mean age was 62 years (range 52–73), and there were 24 males and 4 females. 16 patients had an ECOG status of 1. 6 patients had renal dysfunction. 17 patients had locally advanced disease and 5 had disseminated and locally advanced disease. 6 patients had relapses after radical treatment of the primary tumour. 40 indicator lesions were recorded: 22 lesions were primary tumour, 7 pelvic lymph nodes, 7 lung metastases and 4 extrapelvic lymph nodes.

The total number of courses received by our patients was 89 with a median of 3 (range 1–6). Only 5 patients (18%) completed six cycles. 4 patients withdrew after the first cycle: 1 refused further chemotherapy, 2 had serious protocol violation and 1 had disease progression. 6 patients withdrew after the second

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course, 10 after the third course, 2 after the fourth course and 1 after the fifth course. Of these 19 withdrawals, 18 were because of no response to chemotherapy. 2 non-responders received four and five courses respectively, because computed tomography for response evaluaton was not done after the third cycle.

1 patient with a $T_4N_+M_0$ tumour who attained a PR after the fourth course did not receive further chemotherapy and had radical radiotherapy (60 Gy). He then achieved CR and remained disease-free 53 months after the start of chemotherapy. No patient withdrew because of toxicity.

There were 6 PRs for a response rate of 21% (95% CI 6–36%). 2 patients who responded had lung metastases and 4 locoregional advanced tumour. The mean duration of response was 7 months (range 4–12), excluding the patient who received radical radiotherapy after the fourth course. After carboplatin, 10 patients received doxorubicin and 5-fluorouracil; 1 patient had PR.

No treatment-related deaths occurred. There was no evidence of renal impairment caused by carboplatin nor any neurological toxicity. The most frequent side-effects were nausea, vomiting and myelosuppression (Table 1). 18 patients (64%) had haematological toxicity usually grade I or II; 4 patients had grade III and 1 had grade IV. All 5 severe toxicities were anaemia. 8 patients had grade I or II leukopenia, usually after courses 1–2, and 1 patient had grade II thrombocytopenia after the fourth course.

Thus carboplatin is moderately active in advanced bladder cancer. Other phase II trials gave response rates of 6–24% [7–9]. Carboplatin was well tolerated. Nausea and vomiting were the most frequent side-effects, which should be controllable by standard antiemetics. Myelosuppression was mild except in 5 patients with severe anaemia. Co-existing haematuria probably contributed to this major toxicity. We did not see significant leukopenia or thrombocytopenia, perhaps because the number of courses, (mean 3) was small. Since carboplatin can be administered to patients with poor renal function by dose attenuation and does not require extensive hydration outpatient administration is feasible.

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Epirubicin for Pretreated Advanced Ovarian Cancer

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PROGNOSIS in recurrent epithelial ovarian cancer after chemotherapy with platinum analogues is poor.

In ovarian cancer doxorubicin has moderate activity in untreated patients [1] and has often been included in combination regimens [2]. However, toxicity and reduced activity in patients with platinum-resistant disease limits doxorubicin's value [3]. Epirubicin has similar activity in a variety of tumours [4] and may be less toxic [5]. Epirubicin has some activity in ovarian cancer [6] although as expected this was less in pretreated patients [7]. However, the dose of epirubicin may have been suboptimal since it is now clear that doses over 100 mg/m^2 may be given safely on a 3 weekly schedule. Our aim was to define the activity of epirubicin at the maximum tolerable dose in platinum-resistant ovarian cancer.

21 women with evaluable advanced epithelial ovarian cancer were studied. The median age was 55 (range 38–70). ECOG performance status was 4 patients (grade 0), 11 (grade 1), 5 (grade 2) and 1 (grade 3). All patients had progressed on previous platinum-based chemotherapy within the past 18 months and had bulky (over 2 cm diameter) disease. 18 patients had cystoadenocarcinoma and 3 had an endometroid tumour. Previous treatments were cisplatin (5), carboplatin (19), ifosfamide (5), medroxy-progesterone acetate (1) and radiotherapy (4). Sites of disease were intra-abdominal (21), lymph nodes (4), liver (8), lung (3) and spleen (2).

Epirubicin was given as a 5–10 min intravenous bolus every 21 days on an outpatient basis. Treatment was continued for six courses or until disease progression (or patient refusal). The median number of courses was two (range 1–6) with 4 patients receiving only one course. The starting dose of epirubicin was increased during the study from 90 mg/m^2 (8 patients) to 100 mg/m^2 (1 patient) to 110 mg/m^2 (12 patients). The dose in second and subsequent courses was based on day 10 and day 21 blood counts which allowed for dose reduction or escalation. No patient had the dose increased and 10 of 17 receiving more than one course required a reduction.

Assessment of response was by UICC criteria [8] and survival was calculated from the start of chemotherapy. The WHO scale [9] was used for toxicity.

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