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Letters

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Phase II Trial of Epirubicin at Standard Dose in Relapsed Ovarian Cancer

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THE PROGNOSIS of patients with relapsed ovarian cancer is poor and the role of doxorubicin for their treatment is very limited [1–3]. The results of an analogue, epirubicin, have been more promising as second-line therapy in these patients [4, 5]. From the results of a phase I study of the EORTC Gynaecologic Cancer Cooperative Group with high-dose epirubicin [6] and the preliminary data of a phase II study started in 1990, we began a similar trial, but using a lower dose (standard dose), for better haematological tolerance in this heavily pretreated group of patients.

Eligibility criteria were: pathological proof of epithelial ovarian cancer, prior platinum chemotherapy, no prior use of anthracyclines, no active cardiac disease, performance status (WHO)$\leq$2, age between 18 and 75 years, leucocytes $\geq$4000/mm^3, platelets $\geq$100000/mm^3, bilirubin $\leq$1.2 mg/dl and serum creatinine $\leq$1.2 mg/dl. Informed consent was obtained in all cases. Patients were treated as follows: epirubicin 70–60–50 mg/m^2 on day 1 every 3 weeks depending on the number of prior regimens received (1–2–3 or more, respectively). Routine laboratory analysis and CA-125 were performed on day 1 of each course. Response on therapy was assessed after two courses and WHO criteria were followed to evaluate both response and toxicity. Patient's characteristics are shown in Table 1.

From October 1990 to January 1994, 21 consecutive patients entered this study. All 21 patients were fully evaluable. Median number of courses received per patient was three (range 1–15) with 7 patients at 50 mg/m^2, 2 patients at 60 mg/m^2 and 12 patients at 70 mg/m^2. Evaluation of response was made by CT scan in 14 patients, physical examination in 6 and chest X-ray in 1. There was 1 case of complete response (1 of the 4 potentially platinum-sensitive patients), 2 cases of partial responses (1 of the 10 primary platinum-resistant patients and 1 of the 7 secondary platinum-resistant patients),

Table 1. Patients' characteristics

No. of patients	21
Age (years) median (range)	58 (34–71)
Initial stage	
I_b	1
II_c	2
III_{a-c}	11
IV	7
Histology	
Serous	9
Mucinous	3
Endometrioid	3
Clear cell	1
Undifferentiated	5
Performance status (WHO)	2 (0–2)
No. of prior chemotherapy regimens	1 (1–5)
Response to previous chemotherapy*	
Primary platinum-resistant	10
Secondary platinum-resistant	7
Potentially platinum-sensitive	4

*According to the Markman and Hoskins' classification [8].

4 with stable disease and 14 with progressive disease, for an overall response rate of 14% (3/21). In the platinum-resistant subgroup of patients, the response rate was 11.7% (2/17) (95% confidence interval: 0–26.9%). The three objective responses were treated with 70 mg/m^2 of epirubicin. Median time to progression was 11 weeks (2–46 weeks) and median survival time was 30 weeks (4–79+ weeks). G-CSF was used in 4 patients. Grade 3–4 (WHO) maximum toxicity per patient (% of patients) was: anaemia in 5%, leucopenia 23%, thrombocytopenia in 5% and alopecia in 43%. No toxic death occurred.

In the EORTC trial, that we took as the initial point for our trial, the percentage of responses in the subgroup of patients primary-platinum resistant was 14% (150 mg/m^2, initial dose) [7], close to our results in a similar subgroup of patients (11.7%), with one-third of the dose used in the EORTC study. This therapeutic range is similar to that for hexamethylmelamine, ifosfamide and even paclitaxel which is around 12% [9–11]. With paclitaxel, a 12% response rate in primary platinum-resistant ovarian cancer patients in the European–Canadian trial has been reported [11]. There are only a few studies that had verified the activity of epirubicin, apart from that of the EORTC study already mentioned. Coleman and associates reported no responses in 21 patients who were treated with 90–110 mg/m^2 of epirubicin [12]. Gadducci and colleagues presented a study of epirubicin (120 mg/m^2) associated with lonidamide in 24 patients with a 33.3% response rate [13].

With all these different results obtained from a wide range of doses, the question about the optimal dose of epirubicin in this subgroup of patients is still unanswered and, probably, because of the low chemosensitivity of these patients, it is difficult to demonstrate a dose–response relationship in this setting.

In conclusion, we must include epirubicin in the group of drugs with some activity in relapsed ovarian cancer and, in the platinum-resistant subgroup, its activity seems to be similar to paclitaxel, hexamethylmelamine and ifosfamide. In our opinion, epirubicin should be re-evaluated, in association with cisplatin, in first-line chemotherapy of ovarian cancer.

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Follow-up for Stage 1 Teratoma Surveillance Patients

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DR BRADA in his recent article, "Is There a Need to Follow-up Cancer Patients?" [1] raises important clinical and economic questions regarding future planning of oncology services. Testicular cancer was only briefly mentioned in the article. It is a disease which affects an important group of patients where follow-up is generally thought to be useful clinically. Not only is this disease curable with current therapies, but the development of tumour markers and CT scanning allows recurrent disease to be detected before it is clinically evident. Testicular cancer also affects a group of usually young and employed men, where extensive and time consuming follow-up is costly both to the patients and the Health Service. Is our current tradition of seeing a doctor on each consultation necessary?

We reviewed the management of 54 patients presenting to the Western General Hospital, between January 1986 and December 1990, with Stage 1 teratoma. Of these, 11 patients (20%) were considered to be high risk (greater than two out of four poor histological prognostic factors) and received adjuvant chemotherapy. 9 of the remaining 43 (21%) patients relapsed and received chemotherapy. The average age of these patients was 32 years, 7 months. Of those who relapsed, 82 and 18% did so within the first 6 months and 26 months, respectively (range, 1–26 months; median, 4 months; mean, 7 months 23 days). Relapse was detected by CT scan alone in 4 cases, CT scan and markers in 3 cases, and by markers alone in 2 cases. No cases were detected by clinical examination [2].

From this study, it could be concluded that, since no relapses were detected by clinical examination, follow-up consultations with doctors could be reduced. However, there is still the problem of psychological morbidity. Anxiety usually caused by the threat of recurrence, has been proven to be of clinical significance in a substantial proportion of patients [3–5] and 'reassurance' is considered to be an important function of these clinics. Follow-up visits have been recognised to generate anxiety [6] and result in a feeling of loss of control [7]. In a study of testicular cancer survivors and their relatives, Moynihan [8] found a high level of psychological morbidity, and the two high risk groups were those who were infertile or uncertain of their fertility and those who were unemployed. In a study by Tinkler and associates [9], assessing sexual function after orchidectomy and radiotherapy for testicular cancer, 24% felt disabled by their treatment and this appeared to be related to the presence of only one testicle. They recommended testicular implants.

The psychological effect of follow-up for these patients needs to be studied further, particularly as the clinical value is now questionable. With the answers to these questions, the non-clinical role of a Follow-up Clinic will be clearer and then decisions can be made as to whether or not changes can be made in the organisation of the clinic itself. We know from our initial study that doctors seldom, if ever, identify recurrence themselves. If patients were aware of this, but felt the doctor provided a role in 'reassurance' then a clinic visit is justifiable. However, if we only increase anxiety and alternative arrangements (i.e. regular contact by telephone, surveillance by a trained clinical nurse specialist), as suggested by Dr Brada [1], are considered more suitable and constructive by patients, this may then lead to an improved use of resources and service provided.

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