Eur J Cancer, Vol. 28, No. 2/3, p. 615, 1992.
Printed in Great Britain
0964–1947/92 $5.00 + 0.00

Treatment of Metastatic Testicular Tumours with Bleomycin, Etoposide, Cisplatin and Vincristine

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WE READ with interest the article by Bajorin and Bosl discussing refinements in testicular germ cell tumour therapy (*Eur J Cancer* 27, 677–678). They comment on papers in the same issue by Dearnaley *et al.*, Harland *et al.* and Jansen *et al.* (pp. 684–698). We have reviewed a series of 47 testicular neoplasms at the Queen Elizabeth Military Hospital, Woolwich, London between August 1983 and December 1988 treated with a combination of bleomycin, etoposide, cisplatin and vincristine (BEPV), which has not previously been described. 41/44 of the patients with non-seminomatous germ cell tumours (NSGCT) are alive and disease free with a median follow up of 39 months (range 12–75) from completion of chemotherapy. Deaths occurred in 3/9 men presenting with very large volume disease. 34 were rendered disease free by 4–6 courses of BEPV alone and of the remainder 7 required surgical resection of residual masses from the retroperitoneum.

The regimen consists of a 21 day cycle with cisplatin 50 mg/m^2 given on days 1 and 2, etoposide 120 mg/m^2 on days 1–3. Vincristine 1.4 mg/m^2 is administered on day 1 and bleomycin 15 mg/m^2 on days 2, 9 and 16. The dose of bleomycin is considerably lower than that described in any of the above papers. 33 patients required only four courses of BEPV and so received a total of 180 mg. We had 4 patients with bleomycin lung damage and these were all men that required second line chemotherapy and thus exposure to higher total doses.

Creatinine clearance was reduced after the fourth course of BEPV from 134.5 ml/min to 98.9 ml/min, a drop of 26%. Myelotoxicity was mild and of 204 courses of BEPV given in our series neutropenia cells less than 3000 × 10^6/l occurred on only 38 occasions in 20 patients. Anaemia (haemoglobin less than 9.5 g/l) occurred only six times and thrombocytopenia (platelets below 100 × 10^9/l) was seen on only three occasions. Serious infectious complications were unusual and were virtually confined to those patients with large tumour loads. The vast majority of our patients were servicemen, from whom very high standards of physical fitness are required. This may in some way account for the low incidence of toxicity from BEPV but we believe that the lower dose of bleomycin is an important factor.

We chose to add a vinca alkaloid to a modification of BEP in the hope of producing further improvement to the unsurpassed results of the Royal Marsden series [1]. The decision was based on a certain pragmatism since the vinca alkaloids had previously been shown to be of limited benefit as single agents [2]. Vincristine although ineffective as a single agent has been used with other drugs to intensify treatment [3]. BEPV goes against the vogue to reduce the number of drugs in chemotherapeutic regimes, however, there are conflicting reports as to the efficacy of the two-drug regime of etoposide and cisplatin (EP), as Dr Dearnaley's group point out, and we also remain to be convinced. The work by Harland *et al.* is of interest and the substitution of carboplatin for cisplatin is worthy of serious consideration in our regime for our lower risk patients. We await the findings of the Medical Research Council trial comparing BEP and CEB with anticipation. Finally we would draw attention to the comment made by Barjorin and Bosl that limiting the use of bleomycin has been the objective of several trials in good risk patients. BEPV goes some way to achieving that aim despite bucking the trend to reduce the number of drugs. However, with the continued doubt about EP, we felt that our findings are worthy of mention.

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Revised 14 Nov. 1991; accepted 18 Nov. 1991.

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0964–1947/92 $5.00 + 0.00

Lack of Effect of Tumour Infiltrating Lymphocytes in Patients with Metastatic Melanoma who Failed to Respond to Interleukin 2

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IMMUNOTHERAPY WITH interleukin 2 (IL2) alone induces 20–30% objective responses in melanoma patients [1], but most of these responses are short. To increase specificity, tumour-infiltrating lymphocytes (TIL) from melanoma tumours have been cultured in the presence of IL2 [2, 3]. Rosenberg *et al.* reported 60% responses in patients with metastatic melanoma and 40% responses in patients who did not respond to IL2 [4].

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Received 4 Oct. 1991; accepted 23 Oct. 1991.

Table 1. *Patients' characteristics*

Patients (sex/age)	Site of tumour	Cells injected ($\times 10^9$)	Day of infusion	Response
1 (M/20)	Nodule	12	40	SD (1 month)
2 (M/52)	Nodule	62	40	PD
3 (F/34)	Nodule	150	40	PD
4 (F/36)	Lymph node	86	40	PD
5 (F/42)	Nodule	63	35	SD (1 month)
6 (F/54)	Lymph node	42	35	PD
7 (F/54)	Lymph node	58	30	PD

SD = stable disease, PD = progressive disease.

We have cultured 10 tumour samples from such non-responders to obtain TIL. Only 7 out of 10 patients received a TIL infusion and were evaluable (Table 1). In the 3 non-infused patients, 1 had progressive disease during TIL culture, 1 had two samples cultured at one month without TIL development and, for the third, growth was insufficient. All patients, except 1 (no. 7), had an IL2 infusion ($16 \times 10^6/m^2$ per day) over 4 days starting at the end of the TIL infusion. In general, tolerance was excellent apart from a few chills. 1 patient (no. 5) had an endotoxic shock 6 h after the end of the injection; *Candida parakrusei* was isolated both from blood and cell cultures. As described previously [2, 4] TIL grew easily in samples from melanoma patients but we did not see responses in patients who had failed on IL2.

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Correction

Resistance modification by PSC-833, a novel non-immunosuppressive cyclosporin A. We apologise to Dr P.R. Twentyman and Dr N.M. Bleehen for wrongly adding the letter "A" to cyclosporin in the title and the first line of the abstract in their paper (Vol. 27, 1639–1642).