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Treatment of Good-risk Disseminated Non-seminomatous Germ Cell Tumours: the Less Bleomycin, the More Cisplatin?

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THE SEARCH for continued refinement in the treatment of germ cell non-seminomatous tumour patients has been emphasised [1]. Given the high cure rate achieved through the introduction of cisplatin based chemotherapy, reduction of toxicity is a suitable endpoint in patients with good risk disease. The three-drug regimen BEP (bleomycin, etoposide, cisplatin) is the standard treatment for these patients. Because of the associated pulmonary and vascular toxicity, limiting the use of bleomycin has been the objective of several trials.

So far, two randomised studies compared the efficacy of cisplatin plus etoposide (EP) with or without bleomycin and led to apparently conflicting results [2, 3]. At Indiana University, 178 patients were treated with three cycles of cisplatin (20 mg/m^2) plus etoposide (100 mg/m^2) both given on days 1–5 every 3 weeks, with or without bleomycin (30 IU weekly × 9). The study was suspended early because interim analysis demonstrated a significant ($P = 0.03$) increase in the number of adverse events on EP arm [2]. The second trial was conducted by the EORTC and compared four cycles of cisplatin (20 mg/m^2, days 1–5) plus etoposide (120 mg/m^2, days 1, 3, 5) every 3 weeks, with or without bleomycin (30 IU weekly × 12). In a preliminary analysis, the efficacy of both regimens is not significantly different[3].

Cumulative doses and dose intensities of the drugs delivered in these two trials are detailed in Table 1. The observed divergent results cannot be related to etoposide: the cumulative doses are roughly the same, and the dose intensity is weaker in the EORTC study. Therefore we suggest that the cumulative dose of cisplatin (400 vs. 300 mg/m^2) is the relevant point which may explain the better efficacy of the EP arm in the EORTC trial. The 92% disease-free survival achieved by three cycles of BEP is similar to that observed in patients receiving four cycles of that regimen [4]. Consequently, deleting bleomycin in patients receiving four cycles of etoposide plus cisplatin or limiting the cumulative dose of bleomycin to three cycles of BEP should be two equivalent alternatives.

Table 1. Comparison of cumulative doses and dose intensities of drugs in two randomised trials in good risk non-seminomatous germ cell tumours

			Cisplatin		Etoposide		Bleomycin		
Institution	Protocol		DI	CD	DI	CD	DI	CD	Adverse events
Indiana University	3	BEP	33	300	166	1500	30	270	13/83
	3	EP	33	300	166	1500	0	0	26/83
									$P = 0.03$
EORTC	4	BEP	33	400	120	1440	30	360	14/79
	4	EP	33	400	120	1440	0	0	17/75
									NS

DI = Dose intensities in mg/m^2 per week except for bleomycin (IU per week), CD = cumulative doses in mg/m^2 except for bleomycin (IU), NS = not significant, BEP = bleomycin, etoposide, cisplatin, EP = etoposide, cisplatin.

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Homoeostatic Response Criteria for Cancer Therapy

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THE USE of biological response modifiers such as interferons, interleukins, growth factors and hormones can prolong the duration of remission and survival [1] and improve the neoplastic cell function [2]. In contrast to the cytostatics, these agents stimulate a spectrum of metabolic processes in tumour cells and normal cells. Thus, the traditional assessment of cancer therapy based on tumour reduction may be insufficient in the evaluation of the efficacy of biological response modifiers. The response achieved with these modifiers may be a controlled tumour cell function rather than a tumour reduction. Such a "cytoregulated response" has been shown by Bergström *et al.* who reported a reduction in tumour cell metabolism in meningeoma after treatment with interferon [3] without a simultaneous reduction in tumour size as demonstrated by computed tomography (CT).

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