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Letters

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Comments on: *Veno-occlusive Disease of the Liver in Right Sided Wilms' Tumours*, Tornesello *et al. Eur J Cancer* 1998, 34, 1220–1223

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WE READ with interest the paper recently published by Tornesello and colleagues [1] concerning the possibility of an increased risk of veno-occlusive disease (VOD) in patients with right sided Wilms' tumour (WT).

Hepatic VOD is primarily a clinical diagnosis based on criteria defined by McDonald. These criteria were probably not fulfilled by all the patients with liver toxicity reported in four different studies and included in the analysis performed by Tornesello and colleagues. For instance, only 2 of the 5 patients reported by Raine and associates [2] would meet the VOD criteria (3 children only had hepatomegaly and hypertransaminasaemia).

We earlier published data about hepatic toxicity in patients with WT treated according to the SIOP 9 protocol [3]. In this paper, VOD was defined according to the McDonald criteria [4]. Excluding patients enrolled by the German Paediatric Oncology Group, already included in the Tornesello analysis, and considering only non-irradiated children, we observed 21 cases of hepatotoxicity compatible with VOD in patients with unilateral WT. The tumour originated from the right kidney in 10 children. This was less than 50% of the patients.

Tornesello and colleagues presume that a long standing mass of the right kidney may cause obstruction of blood drainage of the liver. This may damage the intrahepatic vessels. Patients from the SIOP protocol received pre-operative chemotherapy and this usually led to a shrinkage of the tumour and consequently to the resolution of a hypothetical vascular compression. Hepatotoxicity was evident in our patients after a median time of 55 days (range 12–147). This means that in half of our patients toxicity occurred 2 or more months after initiation of chemotherapy. Vascular damage should have been less important by then.

We agree with Davidson and Pritchard [5] that hepatotoxicity in patients treated for WT is different from VOD in the setting of bone marrow transplantation even if all the criteria are met. Why children treated for WT are particularly at risk is not known. Actinomycin-D (AD) dose and schedule are considered risk factors, but the experience we had in the SIOP 9 study seems to indicate that younger age is more important ($P = 0.001$ in a multivariate analysis considering age, AD dose and radiotherapy). In particular, hepatotoxicity compatible with VOD was evident in 16% of children aged less than 1 year versus 6% in the older children.

Furthermore, we want to emphasise that the calculation of AD dose by patient weight instead of body surface led to a mean 25% reduction in the drug dose administered in our study, but this did not significantly protect children from VOD.

In conclusion, vascular compression from right sided WT should be considered in the analysis of future investigations, but it could not explain the occurrence of VOD in most of the patients considered in our study.

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Response from A. Tornesello, S. Mastrangelo and R. Mastrangelo

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WE WISH TO thank G. Bisogno and colleagues for their comments on our paper 'Veno-occlusive disease of the liver in right sided Wilms' tumours'. We agree with A. Davidson, J. Pritchard and G. Bisogno and colleagues that significant

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