because the major objective was to report toxicity not outcome. Our present approach is to use intensive induction and consolidation therapy only for those patients with stage 4 neuroblastoma over the age of 1 year. We agree with Evans *et al.* [1] that the use of other prognostic factors, especially biological features, may allow us to define poor risk neuroblastoma more accurately.

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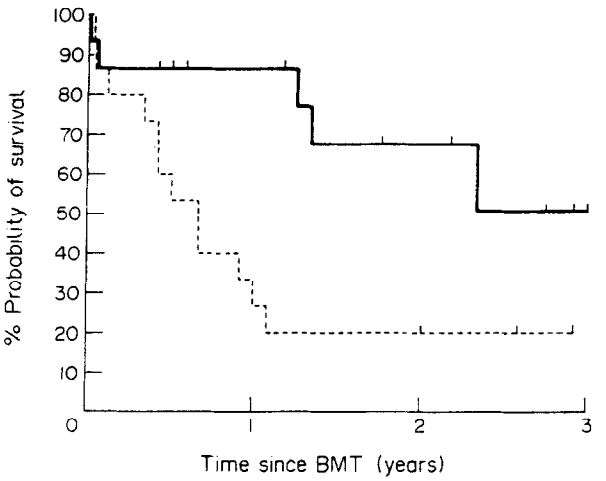

Fig. 1. Overall survival of patients treated with rapid (—) or standard (---) OPEC.

Treatment of Advanced Neuroblastoma

Robin Corbett and Ross Pinkerton

THE REVIEW by Evans *et al.* [1] considers the problems and challenges facing oncologists who treat this aggressive disease and comments specifically on two studies published independently in the same issue of the *European Journal of Cancer* reporting the use of high-dose OMEC (vincristine, melphalan, etoposide and carboplatin) as consolidation treatment in advanced neuroblastoma [1–3]. Evans *et al.* note that there is a significant difference in survival between these two studies and speculate as to the explanation for this. We agree that the differences in scheduling of OMEC (administered over 1 or 5 days) is unlikely to account for the difference. The reviewers enquire about the influence of purging the marrow, although as described in the respective texts this was not done. The criteria for entry into the studies and patient populations treated were also similar.

A possible explanation for the apparent survival difference is the scheduling of the induction regimens employed. 15 of the 16 Newcastle patients received a dose-intense, 10-day rapid scheduling of OPEC (vincristine, cisplatin, etoposide and cyclophosphamide). In contrast, 17/20 patients reported by Corbett *et al.* received standard dose intensity OPEC 3-weekly depending on count recovery. Analysis of the rapid vs. standard OPEC groups (all patients received either schedule of OMEC as consolidation treatment) showed a significant difference ($P < 0.025$) in outcome (Fig. 1, unpublished data). These data are presently being reanalysed to establish whether the significance still holds out.

We would dispute the statement by Evans *et al.* [1] doubting "if any investigator these days would be content to use a single agent for consolidation" and would like to clarify that the reference attesting to the proven efficacy of high-dose melphalan (HDM) is not the report of a pilot study in 1982 by Pritchard *et al.* [4]. The two references clearly cited in the introduction to our article refer to the European Neuroblastoma Study Group (ENSG 1) trial which is the only prospective randomised study of consolidation treatment in neuroblastoma and demonstrates a significantly longer progression-free survival for patients who received HDM [5, 6]. No subsequent published study with any combination chemotherapy or chemoradiotherapy regimen has been proven to have superior results.

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