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Letters

High-dose Consolidation Chemotherapy in Infants with Stage 4 Neuroblastoma

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EIGHTEEN INFANTS (14 boys and four girls) with carefully documented stage 4 neuroblastoma [1] were reported to the European Bone Marrow Transplantation Registry for Solid Tumours by six major European transplant centres between December 1981 and August 1992.

All these patients showed bone metastases on plain radiographs, most confirmed in addition with technetium 99 or ^{123}iodine-meta-iodobenzylguanidine scans. 12 patients (67%) had bone marrow involvement and all had other metastases at distant sites. Tumour cell N-*myc* and DNA ploidy studies are not available. The median age at diagnosis was 9 months (range 1–12 months) and, at the time of high-dose consolidation chemotherapy (HDCHT), 20 months (range 13–27 months). Patients were treated with multiagent induction chemotherapy according to the various national protocols with a median duration of 9 months (range 5–19 months). After induction treatment 7 patients achieved complete remission, 3 very good partial remission and 7 partial remission, while 1 patient had primary refractory disease. Bone marrow infiltration cleared in all patients, but 5/18 still had positive bone lesions on plain radiographs. None of the latter was in the very good partial remission group. HDCHT regimens were melphalan-based in 16/18 and bichloronitrosourea-based in 2/18 patients and were followed by autologous bone marrow rescue (ABMR).

The median follow-up time after HDCHT is 79 months (range 9–127 months). The overall survival from diagnosis at 5 years is 55% for infants and 29% for stage 4 patients older than 1 year of age at diagnosis (P = 0.01)(see Fig. 1). For the 10 complete and very good partial remission patients, the survival rate at 5 years is 77%. HDCHT death rate was 17%.

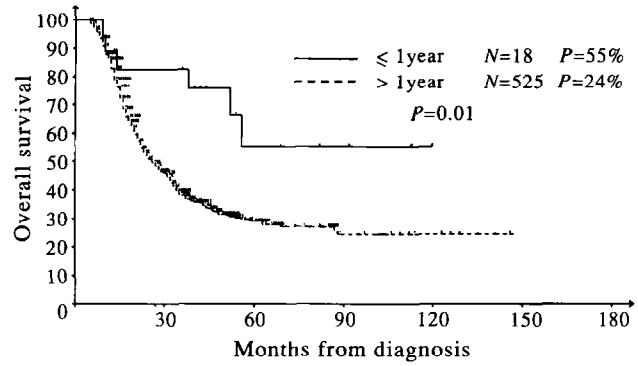

Fig. 1. Stage 4 neuroblastoma, less or greater than 1 year at diagnosis.

There is evidence that rapid progression is associated with N-*myc* amplification [2]. Thus the role of early HDCHT in infants with N-*myc* amplification has still to be defined, but could be considered for infants with initial partial remission (persistant, biopsy-proven bone metastases) or non-responding patients. In view of actuarial survival rates up to 75% [3–5] with conventional dose chemotherapy and surgery these data suggest strongly that there is no advantage in terms of survival when HDCHT and ABMR are given to good responding (bone negative) stage 4 neuroblastoma patients of less than 1 year at diagnosis. Thus, toxicity hazards of such an approach should be avoided in these patients.

1. Brodeur GM, Seeger RC, Barrett A, *et al.* International criteria for diagnosis, staging and response to treatment in patients with neuroblastoma. *J Clin Oncol* 1988, **6**, 1874–1881.
2. Seeger RC, Brodeur GM, Sather H, *et al.* Association of multiple copies of the N-*myc* oncogene with rapid progression of neuroblastoma. *N Engl J Med* 1985, **313**, 1111–1116.
3. Nickerson HJ, Nesbit ME, Grosfeld JL, Baehner RC, Sather H, Hammond D. Comparison of stage IV and IVs neuroblastoma in the first year of life. *Med Pediatr Oncol* 1985, **13**, 261–268.
4. Kretschmar CS, Frantz CN, Rosen EM, Cassady JR, Levey R, Sallan SE. Improved prognosis for infants with stage IV neuroblastoma. *J Clin Oncol* 1984, **2**, 799–803.
5. Paul SR, Tarbell NJ, Korf B, Kretschmar CS, Lavally B, Grier HE. Stage IV neuroblastoma in infants: long-term survival. *Cancer* 1991, **67**, 1493–1497.

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