

Allogeneic Versus Autologous Purged Bone Marrow Transplantation for Neuroblastoma: A Report From the Childrens Cancer Group

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Purpose: We have compared the toxicity, relapse rate, and progression-free survival (PFS) of high-risk neuroblastoma patients receiving identical induction therapy and myeloablative chemotherapy plus total-body irradiation (TBI) followed by allogeneic or autologous purged bone marrow transplantation (BMT).

Patients and Methods: Fifty-six patients with high-risk neuroblastoma underwent BMT at investigator and parent option if they did not have progressive disease after induction chemotherapy with cisplatin, cyclophosphamide, doxorubicin, and etoposide. After surgery and local radiation to residual tumor, myeloablative therapy consisting of etoposide, melphalan, cisplatin, and TBI was given followed by BMT. Patients with human leukocyte antigen (HLA)-compatible siblings received allogeneic bone marrow (n = 20). The remaining patients (n = 36) received autologous bone marrow that had under-

gone multimodality purging and had no remaining detectable tumor cells by immunocytology.

Results: Four of 20 allogeneic patients had a treatment-related death, compared with three of 36 autologous patients (P = .21). The relapse rate among allogeneic BMT patients was 69%, compared with 46% for autologous BMT patients (P = .14). The estimated PFS rates 4 years after BMT were 25% for allogeneic BMT patients and 49% for autologous BMT patients (P = .051).

Conclusion: Overall outcome for patients with neuroblastoma given this same induction therapy followed by autologous purged marrow was similar to that with allogeneic marrow, although bias in patient selection cannot be excluded in a nonrandomized comparison.

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INTENSIVE THERAPY with bone marrow transplantation (BMT) has been tested in patients with high-risk neuroblastoma because of their poor outcome with conventional chemotherapy.¹ Previous reports of both allogeneic and autologous BMT for neuroblastoma have suggested an improved outcome compared with historical controls who received chemotherapy.²⁻⁷ Autologous BMT avoids the problems of graft-versus-host dis-

ease (GVHD) and donor availability, but may result in tumor-cell reinfusion.^{8,9} It has been difficult to compare the outcome for allogeneic and autologous BMT because of patient selection, since, unlike autologous BMT, it is possible to perform allogeneic BMT when the bone marrow has not been cleared of tumor. Differing induction and pre-BMT conditioning regimens, as well as differing time from diagnosis to BMT, have further hindered historical comparisons. We have compared the outcome for two concurrent groups of high-risk neuroblastoma patients who received identical induction chemotherapy, surgery, and local radiation. Patients who remained progression-free at the end of induction, approximately 7 months from diagnosis, received identical myeloablative chemotherapy and total-body irradiation (TBI) followed by either allogeneic or autologous purged BMT.

PATIENTS AND METHODS

Patients

Patients entered onto these two studies were children 1 to 18 years of age at diagnosis of high-risk neuroblastoma. Diagnosis was based on unequivocal pathologic appearance of the tumor or by documentation of bone marrow metastases together with elevated urinary catecholamine metabolites. Initial staging evaluation included computed tomography or magnetic resonance imaging of the primary tumor, bone scan, skeletal survey, and bilateral bone marrow aspirates, biopsies, and immunocytology.¹⁰ High-risk disease was defined by the Childrens Cancer Group (CCG) clinical staging,¹¹ age at diagnosis greater than 1 year, and the pathologic and biologic properties of the tumor as follows: stage IV disease; or stage III disease with any of the following risk features—unfavorable histopathology

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