Abstract

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131I-Metaiodobenzylguanidine with Intensive Chemotherapy and Autologous Stem Cell Transplantation for High-Risk Neuroblastoma. A New Approaches to Neuroblastoma Therapy (NANT) Phase II Study.

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Abstract

^{131}I-Metaiodobenzylguanidine (^{131}I-MIBG) has been used as a single agent or in combination with chemotherapy for the treatment of high-risk neuroblastoma. The activity and toxicity of ^{131}I-MIBG when combined with carboplatin, etoposide, and melphalan (CEM) and autologous stem cell transplantation (SCT) are now investigated in a phase II multicenter study. Fifty patients with MIBG-avid disease were enrolled into 2 cohorts, stratified by response to induction therapy. The primary study endpoint was response of patients with refractory (n = 27) or progressive disease (n = 15). A second cohort of patients (n = 8) with a partial response (PR) to induction therapy was included to obtain preliminary response data. ^{131}I-MIBG was administered on day -21 to all patients, with CEM given days -7 to -4, and SCT given on day 0. ^{131}I-MIBG dosing was determined by pre-therapy glomerular filtration rate (GFR), with 8 mCi/kg given if GFR was 60 to 99 mL/minute/1.73 m^2 (n = 13) and 12 mCi/kg if GFR ≥ 100 mL/minute/1.73 m^2 (n = 37). External beam radiotherapy was delivered to the primary and metastatic sites, beginning approximately 6 weeks after SCT. Responses (complete response + PR) were seen in 4 of 41 (10%) evaluable patients with primary refractory or progressive disease. At 3 years after SCT, the event-free survival (EFS) was 20% ± 7%, with overall survival (OS) 62% ± 8% for this cohort of patients. Responses were noted in 3 of 8 (38%) of patients with a PR to induction, with 3-year EFS 38% ± 17% and OS 75% ± 15%. No statistically significant difference was found comparing EFS or OS based upon pre-therapy GFR or disease cohort. Six of 50 patients had nonhematologic dose-limiting toxicity (DLT); 1 of 13 in the low GFR and 5 of 37 in the normal GFR cohorts. Hepatic sinusoidal obstructive syndrome (SOS) was seen in 6 patients (12%), with 5 events defined as dose-limiting SOS. The median times to neutrophil and platelet engraftment were 10 and 15 days, respectively. Patients received a median 163 cGy (61 to 846 cGy) with ^{131}I-MIBG administration, with 2 of 3 patients receiving >500 cGy experiencing DLT. The addition of ^{131}I-MIBG to a myeloablative CEM regimen is tolerable and active therapy for patients with high-risk neuroblastoma.