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Phase 1 study of mebendazole therapy for refractory/progressive or recurrent pediatric brain tumors

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Abstract

Background: Mebendazole (MBZ) is an anti-helminthic that has shown antitumor activity in mice with gliomas and subsequently in medulloblastoma models. Safety and tolerability have been demonstrated in adults with brain tumors but not explored in children as a monotherapy. We characterized the safety and maximum tolerated dose of oral MBZ in pediatric patients with refractory or progressive brain tumors and assessed progression-free survival (PFS) as a secondary objective.

Methods: Patients up to 21 years of age with refractory or progressive brain tumors were enrolled at 2 centers in a 3 + 3 design with 3 doses of MBZ (1250, 1875, or 2500 mg/m^2/day). MBZ was taken orally 3 times per day and continued until there were signs of toxicity or clinical/radiographic progression. Safety and tolerability were analyzed with descriptive statistics.

Results: There were 17 patients enrolled between 2017 and 2022 with diffuse intrinsic pontine gliomas, high-grade astrocytomas, diffuse midline gliomas, glioblastoma multiform, ependymoma, and nonspecific gliomas. At all 3 dose levels, MBZ was well-tolerated with no dose-limiting toxicities. 121 adverse events (AE) including 69 AEs possibly/probably related to MBZ occurred-the most common being decreased lymphocyte count (n = 6). Six grade 3 (anorexia, dehydration, hypokalemia, increased GGT, blood bilirubin increased, and aspartate aminotransferase increased) and 1 grade 4 (vomiting) were reported. The mean PFS was 7.6 weeks (range of 2 to 24 weeks).

Conclusions: MBZ is safe and tolerable in treating refractory or progressive pediatric brain tumors, with doses up to 2500 mg/m^2/day. There was limited evidence of single-agent efficacy.

Keywords: brain tumors; mebendazole; pediatric; phase 1.