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A phase II study of metronomic oral topotecan for recurrent childhood brain tumors.

Minturn JE, Janss AJ, Fisher PG, Allen JC, Patti R, Phillips PC, Belasco JB.

Division of Oncology, The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, Pennsylvania.

Abstract

BACKGROUND: The prognosis for recurrent or refractory brain tumors in children is poor with conventional therapies. Topotecan is a topoisomerase I inhibitor with good central nervous system (CNS) penetration following oral administration. Increased efficacy of topotecan has been demonstrated with prolonged low-dose daily treatment in pre-clinical models. To investigate further this drug delivered orally in pediatric CNS malignancies, a phase II study in children with recurrent or refractory brain tumors was performed.

PROCEDURE: Patients ≤ 21 years of age at diagnosis with a recurrent, progressive, or refractory primary CNS malignancy and measurable disease, were eligible. Patients enrolled into four strata: ependymoma (N=4), high-grade glioma (HGG) (N=6), brainstem glioma (BSG) (N=13), and primitive neuroectodermal tumor (PNET) (N=8). Oral topotecan was administered once daily at a dose of 0.8 mg/m²/day for 21 consecutive days repeated every 28 days. Response and toxicity profiles were evaluated.

RESULTS: Twenty-six patients were evaluable (median age 9.2 years; 10 males). Two objective responses were observed in PNET patients with disseminated tumor at study entry. These two patients remain alive and in remission 7 and 9.5 years off study. Four other patients (two BSG, one PNET, and one HGG) had stable disease (median 4.6 months). The most common toxicities were hematologic.

CONCLUSIONS: Daily oral topotecan at a dose of 0.8 mg/m²/day can be safely administered to children with recurrent or refractory brain tumors. This regimen identified activity in recurrent PNET. The prolonged progression free survival (PFS) in two PNET patients justifies consideration of this regimen in more advanced clinical trials. *Pediatr Blood Cancer.* 2010;56:39-44. © 2010 Wiley-Liss, Inc.

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