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Phase I Clinical Trial of Cilengitide in Children With Refractory Brain Tumors: Pediatric Brain Tumor Consortium Study PBTC-012

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Purpose: A phase I trial of the antiangiogenesis agent cilengitide (EMD 121974), an alpha v beta 3,5 integrin antagonist, was performed to estimate the maximum-tolerated dose (MTD) and describe dose-limiting toxicities (DLTs) and the incidence and severity of other toxicities when administered to children with refractory brain tumors.

Patients and Methods: Thirty-one assessable patients received intravenous cilengitide over 1 hour twice a week for up to 52 weeks at dosages from 120 to 2,400 mg/m². Serial blood and urine samples for clinical pharmacology studies were obtained in a subset of consenting patients.

Results: No DLTs were observed, and thus, the MTD was not estimated. Three of 13 patients at the dosage level of 2,400 mg/m² experienced grade 3 or 4 intratumoral hemorrhage (ITH) possibly related to the study drug; however, two of the ITH events were asymptomatic and, by the current toxicity criteria, would be classified as grade 1. For patients treated at cilengitide 2,400 mg/m², the 6-month cumulative incidence estimate of ITH is 23% (SE = 13%). No ITH was observed at 1,800 mg/m². Three patients completed 1 year of protocol therapy; one patient with glioblastoma multiforme demonstrated complete response, and two patients had stable disease (SD). An additional patient had SD for more than 5 months.

Conclusion: The phase II dosage of intravenous cilengitide in children with refractory brain tumors is 1,800 mg/m². A phase II trial to assess the efficacy of cilengitide therapy for children with refractory brain tumors is being developed by the Children's Oncology Group.

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Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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