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Cancer Therapy: Clinical

A Phase I Trial of Lenalidomide in Patients with Recurrent Primary Central Nervous System Tumors

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Purpose: Inhibition of angiogenesis represents a promising new therapeutic strategy for treating primary malignant brain tumors. Lenalidomide, a potent analogue of the antiangiogenic agent thalidomide, has shown significant activity in several hematologic malignancies, and therefore we chose to explore its tolerability and activity in patients with primary central nervous system tumors.

Experimental Design: A phase I interpatient dose escalation trial of lenalidomide in patients with recurrent primary central nervous system tumors was conducted.

Results: Thirty-six patients were accrued to the study, of which 28 were evaluable for toxicity, the primary end point of the trial. We show that lenalidomide can be given safely up to doses of 20 mg/m², with the only toxicity being a probable increased risk of thromboembolic disease. Pharmacokinetic studies reveal good bioavailability, linear kinetics, and no effects of enzyme-inducing antiepileptic drugs on the metabolism of lenalidomide. No objective radiographic responses were seen in any of the treated patients. In the group of 24 patients with recurrent glioblastoma, the median time to tumor progression was <2 months and only 12.5% of patients were progression-free at 6 months.

Conclusion: Lenalidomide is well tolerated in patients with recurrent glioma in doses up to 20 mg/m². Treatment may be associated with an increased risk of thromboembolic disease. Preliminary data suggest that single agent activity may be limited in patients with recurrent glioblastoma at the doses evaluated although larger studies will be needed to confirm these observations.