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Phase II Randomized Trial of Lenalidomide in Children With Pilocytic Astrocytomas and Optic Pathway Gliomas: A Report From the Children's Oncology Group

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Abstract

Purpose: Children with low-grade glioma often require long-term therapy and suffer from treatment morbidity. Although targeted agents are promising, tumor targets often encompass normal developmental pathways and long-term effects of inhibition are unknown. Lenalidomide is an immunomodulatory agent with wide-ranging properties. Phase I studies indicated greater tolerability of lenalidomide in children compared with adults and a potential dose-response effect.

Patients and methods: We performed a phase II trial of lenalidomide in children with pilocytic astrocytomas and optic pathway gliomas who failed initial therapy. Primary objectives included determination of objective response rate of children randomly assigned to regimen A, low-dose (20 mg/m^2/dose), or regimen B, high-dose (115 mg/m^2/dose) lenalidomide, and assessment for early progression. Secondary objectives included estimation of event-free survival, overall survival, incidence of toxic events, and assessment of plasma lenalidomide concentrations. Lenalidomide was administered once daily × 21 days of each 28-day cycle for each regimen.

Results: Seventy-four eligible patients were enrolled (n = 37, each arm). The predefined activity level of interest was achieved for both arms. Four objective responses were observed in each arm, and the number of early progressors was low. Eighteen patients completed 26 cycles of therapy (regimen A, n = 12; regimen B, n = 6). The median number of cycles was 14 (range, 2-26) for regimen A and 11 for regimen B (range, 1-26). Of 74 eligible patients who received study drug, 30 required dose reduction for toxicity (regimen A, n = 6; regimen B, n = 24) and 16 discontinued because of toxicity (regimen A, n = 2; regimen B, n = 14).

Conclusion: Lenalidomide demonstrates a sufficient level of activity in children with low-grade glioma to warrant further exploration. Low-dose (20 mg/m^2/dose administered once daily × 21 days of each 28-day cycle) lenalidomide appears to have better tolerability with comparable activity.

Trial registration: ClinicalTrials.gov NCT01553149.