ABSTRACT

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A phase I study of irinotecan and temozolomide with bevacizumab in children with recurrent/refractory central nervous system tumors.

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PURPOSE: Children with relapsed/refractory central nervous system (CNS) tumors require novel combinations of therapies. Irinotecan and temozolomide (IT) is a frequently used therapy with an established toxicity profile. Bevacizumab is an anti-VEGF monoclonal antibody with demonstrated activity in CNS tumors. Therefore, the combination of these agents has therapeutic potential in CNS tumors. The objective of this study was to determine the maximum tolerated dose (MTD) of escalating dose IT combined with a fixed dose of bevacizumab (BIT) in children with relapsed/refractory CNS tumors.

METHODS: A phase I trial was performed in a 3 + 3 design. Therapy toxicities and radiologic responses to treatment were described.

RESULTS: One hundred eighty cycles of therapy were administered to 26 patients. The MTD of BIT was dose level 1, (bevacizumab 10 mg/kg on days 1 and 15, irinotecan 125 mg/m2 on days 1 and 15, and temozolomide 125 mg/m2 on days 1-5 of 28-day cycles). The regimen was well tolerated with primarily hematologic toxicity, which was not dose limiting. Among 22 response-evaluable patients, there was 1 complete response (CR), 6 partial responses (PR), and 10 stable diseases (SD) with an overall response rate (ORR: CR + PR) of 31.8%.

CONCLUSION: At the MTD, BIT therapy was well tolerated, and prolonged treatment courses of up to 24 cycles were feasible, with radiographic responses observed. Further evaluation is needed for efficacy in a phase II trial (NCT00876993, registered April 7, 2009, www.CLINICALTRIALS.gov).

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