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A phase I study of temozolomide and lapatinib combination in patients with recurrent high-grade gliomas.

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Source

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Abstract

We undertook this phase I study to investigate the feasibility of the combination of temozolomide (TMZ) and lapatinib (LP) and to define the maximum tolerated dose (MTD) of LP in patients with relapsed high-grade gliomas. Eligible patients were enrolled in this dose escalation study of LP. TMZ was administered at a fixed dose of 200 mg/m(2) d1-d5 every 28 days. Starting dose of LP was set at 1,000 mg daily continuously, escalated by 250 mg in cohorts of minimum three patients. Translational research investigations were also undertaken in available biopsy material. Between January 2009 and December 2010, 16 patients were entered into the study at three LP levels: 1,000 mg sid (11 patients), 1,250 mg sid (4 patients) and 1,500 mg sid (1 patient). A total of 55 cycles had been delivered. Fourteen patients had stopped treatment because of disease progression, and two because of toxicity. Three patients received 10, 11 and 17 cycles of treatment. Dose-limiting hematological toxicity was observed in 2 patients at the second LP dose level of 1,250 mg sid. MTD was defined at LP 1,000 mg sid. Median progression-free survival (PFS) and survival were 2.4 and 5.9 months, respectively. EGFR amplification and EGFRvIII expression were not related to PFS. Combination of TMZ and LP is feasible with manageable toxicity. The activity of this combination in patients with recurrent glioblastoma multiforme is further investigated in a recently initiated phase II trial.