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No drug holidays in BRAF^{V600E} glioma patients: An argument for dose reduction of targeted therapies

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Abstract

Background: Combined BRAF and MEK inhibition is effective for some BRAF^{V600E}-altered gliomas, a cancer for which there are few effective therapies. While recent clinical trials demonstrate objective response rates of 30%-40%, tolerable adverse event rates are 70%-90%, and 12%-15% of patients stop therapy for toxicity. There are no clear guidelines regarding the timing and reinitiation of BRAF-targeted therapies following drug holidays. Here, we describe 4 patients with rapid disease progression during periods of treatment interruption. All patients experienced a response upon resumption of targeted therapy.

Methods: This is a multi-institutional, retrospective review of 4 patients.

Results: Three patients were diagnosed with BRAF^{V600E} mutated anaplastic pleomorphic xanthoastrocytoma (aPXA) and 1 with epithelioid glioblastoma. The age range was 32 to 46; 3 patients were female and one patient was male. All patients were initially treated with radiation and were subsequently treated with BRAF/MEK inhibitors after disease progression. All patients with aPXA required the targeted therapy to be held due to toxicity and 1 patient held the therapy prior to transitioning to a novel BRAF-targeted agent. All patients were restarted on BRAF/MEK inhibitors after a drug holiday. Three patients required a dose reduction and all improved clinically following reinitiation.

Conclusions: Clinical and radiographic progression may occur rapidly upon holding BRAF-targeted therapy, warranting judicious dose reductions and minimization of drug holidays.

Keywords: BRAF V600E; BRAF inhibitor; MEK inhibitor; drug holiday; glioma.