

Case Reports Neurooncol Pract. 2024 May 24;11(5):660-664. doi: 10.1093/nop/npae046.

eCollection 2024 Oct.

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

Danielle A Bazer^{1, 2}, Anna Kolchinski³, Nancy A O Bush⁴, Jennifer L Clarke⁴, Stephen J Bagley⁵, Karisa C Schreck²

Affiliations

PMID: 39279775 PMID: PMC11398919 (available on 2025-05-24) DOI: [10.1093/nop/npae046](https://doi.org/10.1093/nop/npae046)

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.

© The Author(s) 2024. Published by Oxford University Press on behalf of the Society for Neuro-Oncology and the European Association of Neuro-Oncology. All rights reserved. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

[PubMed Disclaimer](#)