ABSTRACT

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Panobinostat in adults with H3 K27M-mutant diffuse midline glioma: a single-center experience.

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INTRODUCTION: Diffuse midline gliomas (DMG) with the H3 K27M-mutation are a well-described entity with most DMG harboring this mutation, with notable heterogeneity in adults. No therapy has been proven to improve survival in this tumor type. Panobinostat is a histone deacetylase inhibitor that may have therapeutic benefit.

METHODS: We report our retrospective experience with use of panobinostat in adults (> 18 years) with H3 K27M-mutant DMG treated at Mayo Clinic (Rochester) from January 2016 to August 2020, with follow-up until October 2021. Survival was calculated using the Kaplan-Meier method.

RESULTS: 4 patients with H3 K27M-mutant glioma were treated with panobinostat as compassionate use. Patients had a median age of 40 years (range 22-62 years) and 2 were female. Tumor location was midline for all patients, spinal cord (n = 2), brainstem (n = 1), and thalamus (n = 1). All tumors were IDH1/IDH2 wildtype. 3 patients received radiotherapy followed by adjuvant panobinostat. All patients had no other pharmacologic therapy utilized prior to or during panobinostat therapy aside from concurrent dexamethasone utilized in 3 patients. No patient experienced a grade 2 or higher (per CTCAE grade) adverse effect. The median overall survival was 42 months, median progression free survival of 19 months, 2 patients were alive at last follow up (both with spinal cord tumors and received radiation). The best response was stable disease in 2 patients and a partial response in 1 patient.

CONCLUSIONS: This is the first report of clinical outcomes of panobinostat in adults with H3 K27M-mutant DMG. We showed that it is well-tolerated at the dosage schedule that we describe, with no serious adverse effects throughout the study period.

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