Review J Oncol Pharm Pract. 2026 Jun 19:10781552261461529.
doi: 10.1177/10781552261461529. Online ahead of print.

H3K27M-mutant diffuse midline glioma pharmacotherapy: Clinical evidence and practice implications of dordaviprone

Zachary J Nuss [1], Christian DeYoung [2], Derick Gross [3]

PMID: 42317168 DOI: 10.1177/10781552261461529

Abstract

ObjectiveTo evaluate current pharmacotherapeutic strategies for H3 K27M-mutant diffuse midline glioma (DMG), with emphasis on the clinical evidence for dordaviprone, its place in therapy, and its implications for oncology practice.Study Selection and Data ExtractionA structured literature search was conducted using PubMed and ClinicalTrials.gov through November 1, 2025. The search terms "(ONC201 OR dordaviprone) AND ('diffuse midline glioma' OR DMG OR H3 K27 M OR H3K27-altered)" were applied using Boolean operators. Clinical trials, cohort studies, case reports, and relevant preclinical studies evaluating pharmacologic therapies in H3 K27 M DMG were included, with emphasis on clinical outcomes and safety. The review was informed by PRISMA principles and conducted as a narrative review given the limited evidence base. A full systematic review was not possible given the limited and heterogeneous evidence base.ResultsDordaviprone received accelerated FDA approval based on the results of an integrative analysis of five phase 1 and 2 trials. The primary endpoint of overall response rate (ORR) was 20%, disease control rate 40%, and median duration of response (DOR) was 11.2 months. Fatigue, headache, vomiting, and nausea are the most common adverse effects.DiscussionDordaviprone is the only FDA approved medication for H3 K27 M DMG. It demonstrates long-lasting radiographic and symptomatic improvement. It is currently approved for recurrence following prior therapy, not as a substitute for radiation or surgery. The ACTION trial may provide guidance on its broader use in newly diagnosed H3 K27 M DMG. Pharmacists play a role in optimizing treatment, monitoring safety and drug interactions, and supporting patient adherence.ConclusionDordaviprone is a novel treatment option with modest response rates and durable benefit in recurrent/progressive H3 K27 M DMG. Ongoing trials may further define its role in earlier lines of therapy.

Keywords: H3K27M; ONC201; Oncology; diffuse midline glioma; dordaviprone; drug interactions; imipridone; neuro-oncology; pharmacotherapy; targeted therapy.