

RESEARCH SUMMARY

Vorasicidenib in IDH1- or IDH2-Mutant Low-Grade Glioma

Mellinghoff IK et al. DOI: 10.1056/NEJMoa2304194

CLINICAL PROBLEM

Gliomas, the most common malignant primary brain tumor type in adults, are categorized by histologic and molecular features and by tumor grade. Almost all grade 2 gliomas have mutations in the genes encoding the metabolic enzymes isocitrate dehydrogenase 1 (IDH1) or 2 (IDH2).

CLINICAL TRIAL

Design: This phase 3, double-blind, randomized, placebo-controlled trial tested the clinical effects of vorasicidenib — an oral brain-penetrant inhibitor of mutant IDH1 and IDH2 enzymes — in patients with residual or recurrent grade 2 IDH-mutant glioma who had undergone surgery as their only previous treatment.

Intervention: 331 patients were assigned to receive oral vorasicidenib (40 mg once daily) or matched placebo in 28-day cycles. The primary end point was imaging-based progression-free survival.

RESULTS

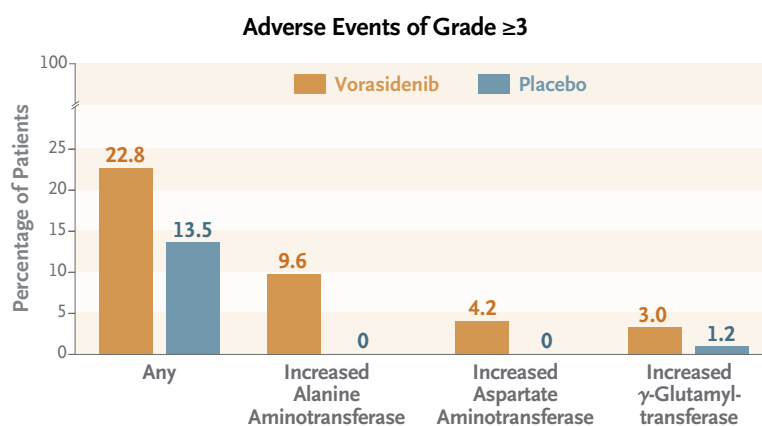
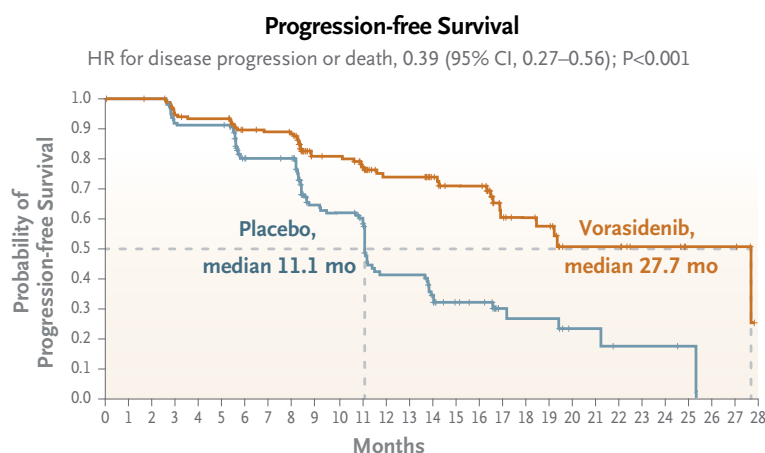
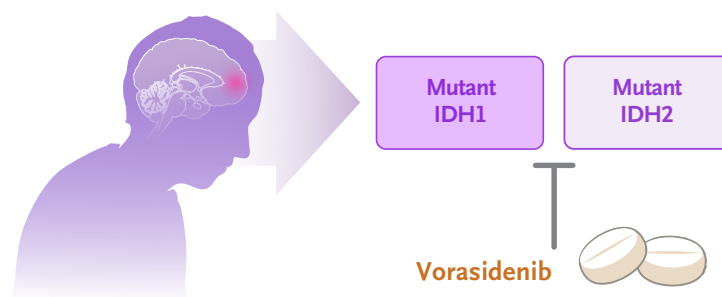
Efficacy: Progression-free survival was significantly longer with vorasicidenib than with placebo.

Safety: Although most adverse events with vorasicidenib were mild, events of grade ≥ 3 were more frequent with vorasicidenib than with placebo; the most common was an increase in alanine aminotransferase level. Serious adverse events that were determined by the investigators to be related to the trial drug or placebo occurred in 1.8% of vorasicidenib recipients and in no placebo recipients.

LIMITATIONS AND REMAINING QUESTIONS

- Patients with high-risk features were excluded from the trial.
- Additional end points, including health-related quality of life and neurocognition, were not reported.
- Results for the overall survival end points remain to be determined.

Links: [Full Article](#) | [NEJM Quick Take](#) | [Editorial](#) | [Science behind the Study](#)



CONCLUSIONS

Among patients with grade 2 IDH-mutant glioma, progression-free survival was significantly longer with vorasicidenib than with placebo.