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

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RESEARCH SUMMARY

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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 vorasidenib — 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 vorasidenib (40 mg once daily) or matched placebo in 28-day cycles. The primary end point was imaging-based progression-free survival.

RESULTS

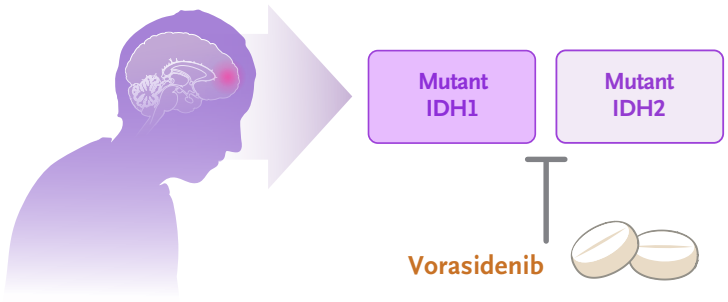
Efficacy: Progression-free survival was significantly longer with vorasidenib than with placebo.

Safety: Although most adverse events with vorasidenib were mild, events of grade ≥3 were more frequent with vorasidenib 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 vorasidenib recipients and in no placebo recipients.

LIMITATIONS AND REMAINING QUESTIONS

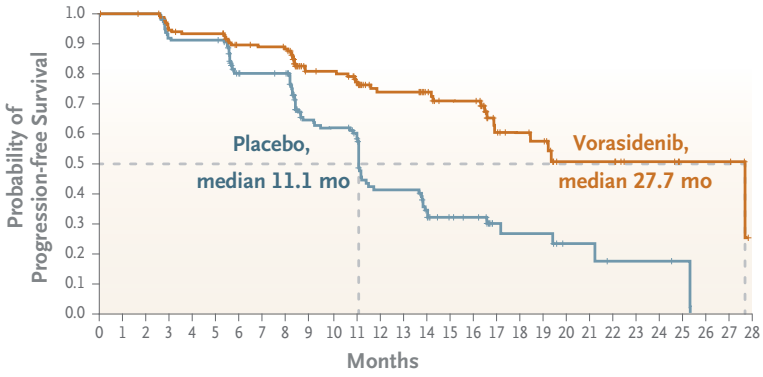
- Patients with high-risk features were excluded from the trial.
- Additional end points, including health-related quality of life and neurocognition, were not reported.
- Results for the overall survival end points remain to be determined.

Links: Full Article | NEJM Quick Take | Editorial | Science behind the Study

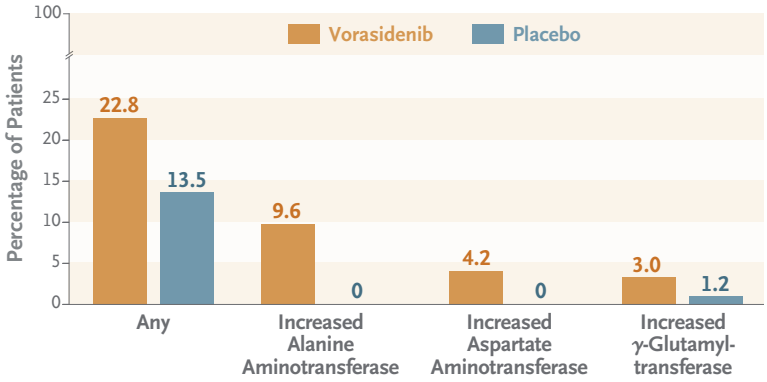


Progression-free Survival

HR for disease progression or death, 0.39 (95% CI, 0.27–0.56); P<0.001



Adverse Events of Grade ≥3



CONCLUSIONS

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