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Efficacy of Adding Veliparib to Temozolomide for Patients With MGMT-Methylated Glioblastoma: A Randomized Clinical Trial

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Abstract

Importance: The prognosis for patients with glioblastoma is poor following standard therapy with surgical resection, radiation, temozolomide, and tumor-treating fields.

Objectives: To evaluate the combination of veliparib and temozolomide in glioblastoma based on preclinical data demonstrating significant chemosensitizing effects of the polyadenosine diphosphate-ribose polymerase 1/2 inhibitor veliparib when combined with temozolomide.

Design, setting, and participants: Patients with newly diagnosed glioblastoma with MGMT promoter hypermethylation who had completed concomitant radiation and temozolomide were enrolled between December 15, 2014, and December 15, 2018, in this Alliance for Clinical Trials in Oncology trial. The data for this analysis were locked on April 21, 2023.

Interventions: Patients were randomized and treated with standard adjuvant temozolomide (150-200 mg/m² orally, days 1-5) combined with either placebo or veliparib (40 mg orally, twice daily, days 1-7) for 6 cycles.

Main outcomes and measures: The primary end point for the phase 3 portion of the trial was overall survival (OS).

Results: There were 322 patients randomized during the phase 2 accrual period and an additional 125 patients randomized to complete the phase 3 accrual, for a total of 447 patients in the final phase 3 analysis. The median (range) age for patients was 60 (20-85) years and 190 patients (42.5%) were female. The median OS was 24.8 months (90% CI, 22.6-27.7) for the placebo arm and 28.1 months (90% CI, 24.3-33.3) for the veliparib arm (P = .17). The difference in survival did not meet the prespecified efficacy end point. However, there was a separation of the survival curves that favored the veliparib arm over 24 to 48 months of follow-up. The experimental combination was well tolerated with an acceptable elevation in grade 3 or 4 hematologic toxic effects.

Conclusions and relevance: This trial found that adding veliparib to adjuvant temozolomide did not

significantly extend OS in patients with newly diagnosed, MGMT-hypermethylated glioblastoma.

Trial registration: ClinicalTrials.gov Identifier: [NCT02152982](https://clinicaltrials.gov/ct2/show/study/NCT02152982).

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