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Phase 2 Trial of Veliparib, Local Irradiation and Temozolomide in Patients with Newly Diagnosed High-Grade Glioma: A Children's Oncology Group Study

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Abstract

Background: The outcome for pediatric patients with high-grade glioma (HGG) remains poor. Veliparib, a potent oral poly(adenosine diphosphate-ribose) polymerase (PARP) 1/2 inhibitor, enhances the activity of radiotherapy and DNA-damaging chemotherapy.

Methods: We conducted a single-arm, non-randomized phase 2 clinical trial to determine whether treatment with veliparib and radiotherapy, followed by veliparib and temozolomide, improves progression-free survival in pediatric patients with newly diagnosed HGG without H3 K27M or BRAF mutations compared to patient level data from historical cohorts with closely matching clinical and molecular features. Following surgical resection, newly diagnosed children with non-metastatic HGG were screened by rapid central pathology review and molecular testing. Eligible patients were enrolled on Stratum 1 (IDH wild-type) or Stratum 2 (IDH mutant).

Results: Both strata were closed to accrual for futility after planned interim analyses. Among the 23 eligible patients who enrolled on Stratum 1 and received protocol therapy, the 1-year event-free survival (EFS) was 23% (standard error, SE = 9%) and 1-year overall survival (OS) was 64% (SE = 10%). Among the 14 eligible patients who enrolled on Stratum 2 and received protocol therapy, the 1-year EFS was 57% (SE = 13%) and 1-year OS was 93% (SE = 0.7%).

Conclusions: Rapid central pathology review and molecular testing for eligibility was feasible. The protocol therapy including radiation, veliparib and temozolomide was well tolerated but failed to improve outcome compared to clinically and molecularly matched historical control cohorts treated with higher doses of alkylator chemotherapy.

Keywords: High grade glioma; clinical trial; glioblastoma; temozolomide; veliparib.