PURPOSE: To study the efficacy and tolerability of VPA and radiation, followed by VPA and bevacizumab in children with newly diagnosed DIPG or HGG. METHODS: Children 3-21 years of age with newly diagnosed DIPG or HGG were enrolled. Concurrent with radiation therapy, VPA was initiated at 15 mg/kg/day divided tid and dose-adjusted to maintain a trough range of 85-115 mcg/ml. VPA was continued post-XRT, and bevacizumab was started at 10 mg/kg bi-weekly four weeks after completing XRT. RESULTS: From September 2009 through December 2015, 20 DIPG and 18 HGG patients were enrolled. During radiation and VPA, grade-3 or higher toxicities included grade-5 tumor edema (1), grade-3 neutropenia (1), and grade-3 thrombocytopenia (1). During VPA and bevacizumab, the most common grade-3 or higher toxicities requiring treatment modifications were grade-3 thrombocytopenia (4), grade-3 weight gain (4), and grade-3 hypertension (3). Two patients discontinued protocol therapy prior to disease progression for grade-4 thrombosis (1) and grade-1 intra-tumoral hemorrhage (1). Median PFS and OS for DIPG were 7.9 (95% CI 5.4-8.1) and 10 (7.1-12.9) months, and estimated 1-year PFS was 13% (2-33%). Median PFS and OS for HGG were 8.7 (3.9-10.6) and 11 (7.7-21.2) months, and estimated 1-year PFS was 21% (5-45%). Of note, 3 patients with glioblastoma and mismatch-repair deficiency syndrome, predicted to have resistance to alkylator agents, received protocol therapy for 9, 10.4, and 16.7 months. CONCLUSION: Addition of VPA and bevacizumab to radiation was well-tolerated but did not appear to significantly improve PFS or OS in children with DIPG or HGG.