Children and young adults (≤39 y/o) newly-diagnosed with HGG, including DIPG with Biopsy/resection tissue

Comprehensive Molecular Characterization for eligibility and TarGeT arm assignment involves testing for the presence of genetic alterations*

Cell cycle or PI3K/AKT/mTOR alteration	MAPK pathway alteration	ACVR1 mutation	IDH1 mutation	PDGFRA mutation	Replication/ Repair Deficient	None of the other alterations	
						H3K27-wildtype	H3K27-altered
A	B	C	D	E	F	G	K
		+TP-0184	± TMZ				
Ribocciclib + Everolimus	DAY101 + Pimasertib	TP-0184 + Trametinib	Olutasidenib + TMZ	Avapritnib	Nivolumab + Relatlimab	Nivolumab + Decitabine	ACT001
Pathogenic alterations that activate cell cycle and/or PI3K/mTOR pathway: **Cell cycle:** • CDK4/6 amp • CDKN2A/B/C deletion • CCND1/2 amp **PI3K/mTOR pathway:** • PTEN del or mut • PIK3CA but or amp +exclude patients w/biallelic RB1 loss	Pathogenic alterations presumed to activate MAPKinase pathway: • PRAF V600E/D/K • Other RAF but or fusion • KRAS, NRAS mut or amp • NF1 del or mut	ACRV1 mutation	IDH1R12 H/C/G/S/L mutation	PDGFRA mutation or amplification	Tumor mutational burden ≥10mut/mb and/or Lynch syndrome, CMMRD, PPD, confirmed by gremlin testing		H3 K27M or K27I mutation (or EGFR alteration/ amp or methylation consistent w/ DMG and loss of H3K27me3 by IHC

RADIATION THERAPY

* If patients are eligible for more than one arm, final arm assignment will be decided by the molecualr screening committee

Correlative Research

Genomic and immunologic profiling of blood, CSF, and tumor tissue, as well as neuroimaging and patient reported outcomes to determine longitudinal biomarkers to predict response, recurrence, and/ or resistance

Integration of Longitudinal Clinical Response, Genomic, Immunologic, Neuro-Imaging, and Patient-reported Outcomes Data