possibility of cancer predisposition; the HGG was hypermutated with germline PMS2 mutation confirming diagnosis of CMMRD. Near total resection was undertaken followed by focal radiotherapy 54 Gy, with 1 cycle of concomitant CCNU. MRI post radiotherapy showed tumour progression. Anti-PDl inhibitor Nivolumab was commenced. CTLA-4 antibody, Ipilimumab was added after 4 cycles of Nivolumab due to poor response. Tumour response was seen, but dual therapy had to be discontinued due to toxicity. The tumour progressed following further single agent Nivolumab. In view of multiple mutations in the mTOR pathway (NF1, PIK3/PTEN, TSC1, TSC2), a mTOR inhibitor, Everolimus was commenced. There was 25% tumour reduction after 4 weeks treatment and further reduction after 6 months. Resection of residual tumour showed necrotic tissue only. There continues to be a sustained response to Everolimus for over 12 months. **DISCUSSION:** Approximately a third of CMMRD HGG respond to checkpoint inhibitors. For those that don't, these hypermutated tumours offers the possibility of targeting specific molecular pathways. Response to Everolimus in HGG harbouring mTOR aberrations have been described. To our knowledge this is the first report of successful use of mTOR inhibitor in CMMRD HGG. **CONCLUSION:** Targeted molecular treatment for patients with CMMRD hypermutated brain tumours should be considered according to the mutated pathways.

HGG-33. PROGNOSTIC FACTORS OF H3K27M HISTONE-MUTANT DIFFUSE MIDLINE GLIOMAS IN PATIENTS ≤18YRS

Qingjun Hu, Mingyao Lai, Juan Li, Linbo Cai; Guangdong Sanjiu Brain Hospital, Guangzhou, Guangdong, China

OBJECTIVE : Diffuse midline gliomas associated with high malignancy and poor prognosis. The primary treatment modalities include surgery, radiotherapy and chemotherapy. The purpose of this study was to investigate the prognostic factors of diffuse intracranial midline glioma. METHODS: A retrospective analysis was performed on 44 cases younger than 18 yrs of H3K27M histone-mutant diffuse midline gliomas diagnosed in Guangdong Sanjiu Brain Hospital from November 2017 to November 2021. The median age was 9 years (range:3-18), including 24 males and 20 females, lesions located in thalamus were 9, while in brain stem were 35. Treatment methods: 35 cases received radiotherapy, 9 cases did not. Among the patients who received RT, 26 cases with concurrent chemoradiotherapy + adjuvant chemotherapy, 8 cases with concurrent chemoradiotherapy only, and 1 case only with radiotherapy. Kaplan-meier method was used to calculate overall survival (OS), and log-rank test was used to test. $P < 0.05$ was considered statistically significant. RESULTS: By January 27, 2022, 13 cases survived, 25 cases died, and 6 cases were lost to follow-up. The median survival time of 44 patients was 6.95 months (range : 1-23.5 months). The median survival was 8.4 months in the radiotherapy group vs 3.7 months in the non-radiotherapy group ($P < 0.001$); The median survival time of radiotherapy without adjuvant chemotherapy vs radiotherapy with adjuvant chemotherapy was 6.2 months vs 9.35 months (P=0.479). CONCLUSION: Radiotherapy can prolong the survival time of diffuse midline glioma in children with H3K27M histone mutant but no survival benefit was observed in patients with concurrent chemotherapy.

HGG-34. UPFRONT MOLECULAR TARGETED THERAPY FOR THE TREATMENT OF BRAF-MUTANT PEDIATRIC HIGH-GRADE GLIOMA

Tom Rosenberg[1], Kee Kiat Yeo[1], Audrey Mauguen[2], Sanda Alexandrescu[3], Sanjay P. Prabhu[4], Jessica W. Tsai[1], Seth Malinowski[5], Mrinal Joshirao[6,7], Karishma Parikh[7], Sameer Farouk Sait[7], Marc K. Rosenblum[8], Jamal K. Benhamida[8], George Michaiel[9], Hung N. Tran[10], Sonika Dahiya[11], Kara Kachurak[12], Gregory K. Friedman[12], JulieI. Krystal[13], Michael A. Huang[14], Ashley S. Margol[9], Karen D. Wright[1], Dolly Aguilera[15], Tobey J. MacDonald[15], Susan N. Chi[1], Matthias A. Karajannis[7]; [1]Dana Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA, USA. [2]Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [3]Department of Pathology, Boston Children's Hospital, Boston, MA, USA. [4]Department of Radiology, Boston Children's Hospital, Boston, MA, USA. [5]Department of Oncologic Pathology, Dana-Farber Cancer Institute, Boston, MA, USA. [6]SUNY Downstate Medical Center, Brooklyn, NY, USA. [7]Pediatric Neuro-Oncology Service, Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [8]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA. [9]Cancer and Blood Disease Institute at Children's Hospital Los Angeles and Keck School of Medicine at University of Southern California, Los Angeles, CA, USA. [10]Kaiser Permanente Southern California, Los Angeles, CA, USA. [11]Washington University School of Medicine, St. Louis, MO, USA. [12]Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, USA. [13]Cohen Children's Medical Center, New Hyde Park, NY, USA. [14]Norton Children's Hospital/Affiliate of University of Louisville School of Medicine, Louisville, KY, USA. [15]Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA, USA

BACKGROUND: The prognosis for pediatric high-grade glioma (pHGG) is poor despite aggressive multi-modal therapy. Objective responses to targeted therapy with BRAF inhibitors have been reported in some patients with recurrent BRAF-mutant pHGG but are rarely sustained. METHODS: We performed a retrospective, multi-institutional review of patients with BRAF-mutant pHGG treated with off-label BRAF +/- MEK inhibitors as part of their initial therapy. RESULTS: Nineteen patients were identified, with a median age of 10.7 years (range: 1.8–20.3). Histologic diagnoses included HGG (n=6), glioblastoma (n=3), anaplastic ganglioglioma (n=4), diffuse midline glioma (n=3), high-grade neuroepithelial tumor (n=1), anaplastic astrocytoma (n=1), and anaplastic astroblastoma (n=1). Recurrent concomitant oncogenic alterations included CDKN2A/B loss, H3 K27M, as well as mutations in ATRX, EGFR and TERT. Eight patients received BRAF inhibitor monotherapy. Eleven patients received combination therapy with BRAF and MEK inhibitors. Most patients tolerated long-term treatment well with no grade 4–5 toxicities. Objective and durable imaging responses were seen in the majority of patients with measurable disease. At a median follow-up of 2.3 years (range,0.3–6.5), three-year progression-free (PFS) and overall survival (OS) for the cohort were 65% and 82%, respectively, and superior to a historical control cohort treated with conventional therapies. CONCLUSIONS: Upfront targeted therapy for patients with BRAF-mutant pHGG is feasible and effective, with superior clinical outcomes observed compared to historical data. This promising treatment paradigm is currently being evaluated prospectively in the Children's Oncology Group ACNS1723 clinical trial.

HGG-35. RADIATION INDUCED HIGH GRADE GLIOMAS: A SINGLE CENTER EXPERIENCE

Mrinal Joshirao[1,2], Sameer Farouk Sait[1], Nancy Bouvier[1], Katherine Hill[1], Yasmin Khakoo[1], Kim Kramer[1], Stephen Gilheeney[1], Suzanne Wolden[1], Craig Nolan[1], Lauren Schaff[1], Marc Rosenblum[1], Tejus A. Bale[1], Jonathan T. Yang[1], Andrew Lin[1], Ira J. Dunkel[1], Matthias Karajannis[1]; [1]Memorial Sloan Kettering Cancer Center, New York, New York, USA. [2]SUNY Downstate Health Sciences University, Brooklyn, New York, USA

INTRODUCTION: Patients receiving cranial radiotherapy (RT) are at risk for a subsequent radiation-induced glioma (RIG). RIGs are rare, generally develop with a latency of 2 years to several decades, display high-grade histology and an aggressive clinical course with poor prognosis. METHODS: We retrospectively analyzed patients with a diagnosis of RIG seen at our institution from 2001-2021, analyzing clinical, histological, molecular, and genetic characteristics. RESULTS: Twenty-one patients (n=15 male) with a history of ALL (n=6), medulloblastoma (n=5), germ cell tumors (n=4), or other (n=6) diagnosed at a median age of 8.3 years (range 1.6 to 36.4) were identified. Median age at RIG diagnosis was 18 years (range 7.8 to 66.9). Prior RT was focal+craniospinal (n=7), whole brain (n=5), total body (n=3), focal (n=1), or unknown (n=5). Median radiation dose received was 2,340 cGy (range 1,200 to 5,400). The median time from RT to RIG diagnosis was 7.7 years (range 1.6 to 23.8). All RIGs were histologically high grade (WHO Grade III or IV). Immunohistochemistry did not reveal IDH(R132H) (n=9) or H3K27M (n=8) in any tumor. Some tumors demonstrated loss of expression of ATRX (1/9) and/or H3K27me3 (3/6), and/or strong diffuse expression of p53 (0/3). Targeted panel sequencing (n=10) revealed recurrent somatic alterations including CDKN2A/B, PDGFRa/KIT/KDR, TEK, MTAP, ATM and NF1. Germline alterations were detected in 4/12 patients (pathogenetic variants in ATM, CHEK2, HOXB13 and NF1). With median follow-up of 4.5 years, two-year PFS and OS for the cohort (n=20) were 10% and 44% respectively. Two patients (with anaplastic oligodendroglioma and anaplastic astrocytoma) are alive without progression 5.4 and 13.6 years after diagnosis following surgery, RT and chemotherapy. CONCLUSION: Although RIGs are associated with a poor prognosis, they are not always fatal. Our findings suggest aggressive therapy should be considered for these patients.

HGG-36. ELUCIDATING THE ROLE OF LONG NON-CODING RNAS IN PEDIATRIC HIGH GRADE GLIOMAS

Jessica W Tsai[1,2], Frank PB Dubois[2,3], Dayle K Wang[1], Alexander Crane[2,3], Alexandra L Condurat[1,2], Brian Krug[4,5], Adam Brown[2], John G Doench[2], Nada Jabado[4,5], Pratiti Bandopadhayay[1,2]; [1]Department of Pediatric Oncology, Dana-Farber Boston Children's Cancer and Blood Disorders Center, Boston, MA, USA. [2]Broad Institute of MIT and Harvard, Cambridge, MA, USA. [3]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA. [4]Department of Human Genetics, McGill University, Montreal, Canada. [5]Department of Pediatrics, McGill University, The Research Institute of the McGill University Health Centre, Montreal, Canada

BACKGROUND: Genomic and transcriptomic studies have elucidated new insights into the landscape of diffuse intrinsic pontine glioma (DIPG). However, the role of long non-coding RNAs (lncRNAs) has not been explored at depth in these tumors, and there have not been studies focused on how lncRNAs interact with the K27M histone mutation. In a recent analysis of nearly 200 DIPGs and pediatric high-grade gliomas (pHGG), we previously detected a novel, recurring structural variant in the lncRNA CCDC26. This rearrangement occurs in nearly 10% of all DIPGs, and we