Abstracts

of KIAA1549-BRAF fusion or BRAF V600E mutation within PMA and PA correlates with classic qualitative imaging characteristics.

LGG-11. INSTITUTIONAL EXPERIENCE OF BRAF TARGETING THERAPY
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BACKGROUND: The use of BRAF inhibitors is widely accepted in adult oncology as treatment for BRAF mutated cancers. BRAF alterations are frequently found in both pediatric low grade and high-grade gliomas, which has opened a new door to targeted therapies for pediatric gliomas. Targeted therapy drugs are associated with predictable patterns of adverse events. However, treating in children may potentiate unique challenges. We present our institutional experience of targeted therapy with a focus on adverse events.

METHODS: We conducted a retrospective chart review of patients treated with BRAF and/or MEK inhibitors between 2015–2019. RESULTS: There are nine patients treated with either MEK inhibitor (n=6) or the combination therapy (n=3). The most common diagnosis was Pilocytic astrocytoma. Targeted therapy was chosen as salvage therapy in all patients. The most common side effect was a pruritic erythematous rash, observed in 8 out of 9 patients. Cardiac toxicity (Grade 2, n=1) and GI toxicity (Grade 3, n=1) were found in patients treated with MEK inhibitor. Both cases resulted in cessation of therapy or significant decreased dose respectively. While two patients died due to progression of disease and two other continued to progress, 5 patients have demonstrated stable disease while on therapy. CONCLUSIONS: Our data supports the use of trametinib for both upfront and relapsed/refractory pediatric low grade gliomas with acceptable toxicity.

LGG-12. TRAMETINIB FOR PEDIATRIC LOW GRADE GLIOMAS: A SINGLE INSTITUTION EXPERIENCE
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INTRODUCTION: Low grade gliomas (LGG) are the most common pediatric brain tumors. Tumors not amenable to resection can recur or progress despite treatment with chemotherapy and/or radiation. Recent discovery of the activation of the mitogen-activated-protein-kinase (MAPK) pathway as the primary oncogenic driver for this group of tumors has led to a shift towards the use of BRAF and MEK inhibitors. METHODOLOGY: Herein, we performed a chart review of seven pediatric LGG treated with trametinib, a MEK inhibitor. While most were treated in the relapse setting, one patient was treated for de novo LGG as a result of experiencing multiple severe adverse effects to conventional agents. RESULTS: Median age was 14 years old (range: 5 to 17 years). Six of seven patients had tissue for molecular characterization. The 2 patients with Neurofibromatosis Type 1 (NF-1) carried no other molecular aberrations. Two had the BRAF V600e mutation (1 had concurrent with BRAF (n=1) and 1 with concurrent RAF1 (n=1) mutation) and 1 had concurrent KIAA1549: BRAF fusion. Average duration on treatment was 8 months (range: 3 to 31 months). Disease control was achieved in 6 of 7 subjects, with one PR as best response. One patient with concurrent BRAF V600e and PTEN11 mutations progressed on trametinib and was switched to dual BRAF and MEK inhibitor therapy. Most common toxicities were acne (57.1%), oral mucositis (42.9%), skin rash, and paronychia (both 28.6%). Three patients required dose reduction and/or intermittent dose interruption. CONCLUSION: Our data supports the use of trametinib for both upfront and relapsed/refractory pediatric LGG.

LGG-13. THE CLINICAL AND MOLECULAR LANDSCAPE OF GLIOMAS IN ADOLESCENTS AND YOUNG ADULTS
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OBJECTIVE: Pediatric low grade gliomas are typically driven by MAPK upregulation with excellent long-term survival. In contrast, adult lower grade gliomas commonly harbor IDH1 mutations and undergo malignant transformation. Gliomas in adolescents and young adults (AYA) are an orphan group of tumors that have been poorly described. We aim to determine the clinical and molecular landscape of AYA gliomas. METHODS: A multi-institutional population based cohort of 839 patients diagnosed with glioma between 15–40 years has been identified. Complete molecular analysis, long term outcome and therapeutic data are being collected. RESULTS: Of 364 AYA gliomas analyzed, the prevalence of WHO grade I tumors was highest in the <12 (61%, 54%), while the prevalence increased in WHO grade II-IV tumors in contrast, BRAF alterations were most frequently observed in WHO grade I and II tumors and enriched in those less than 20 years. Five-year progression-free survival for BRAF v. p600E and IDH1 p.R132H were 81%, 76% respectively. Mutations were observed in H3F3A (57%), p.G34R, gliomas (p=0.0001). CONCLUSIONS: Gliomas in AYA overlap pediatric and adult classification and exhibit enrichment for pediatric alterations. The latter are associated with improved PFS and are amenable to targeted therapies, this should be considered in the work up of these tumors.

LGG-14. MULTI-OMIC ANALYSIS OF MAPK ACTIVATION IN PEDIATRIC PILOCYTIC ASTROCYTOMA
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Pilocytic astrocytomas (PA) are low-grade gliomas (pLGG) and are the most frequent childhood brain tumors. They are characterized by oncogene- and tumor-specific signatures (OSSs) that underlie tumor heterogeneity. Here we present a multi-omic analysis of PAs. The aim of this study was to investigate how PA OSSs evolve during tumor progression, to identify potential drivers of tumor progression, and to dissect potential therapeutic targets. METHODS: We performed a multi-omic analysis of 56 PA samples. We combined transcriptome and proteome data from PA samples with a normal human brain and evaluated the evolution of OSSs from low-grade to high-grade lesions. RESULTS: We identified a shift towards the use of BRAF and MEK inhibitors. Our data supports the use of trametinib for both upfront and relapsed/refractory pediatric low grade gliomas with acceptable toxicity.

LGG-15. RETROSPECTIVE ANALYSIS OF CHILDREN WITH LOW-GRADE GLIOMAS TREATED IN KING FAHAD MEDICAL CITY KFMC-SINGLE INSTITUTIONAL EXPERIENCE
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This study presents a retrospective single-institutional experience of children with low-grade gliomas treated in King Fahad Medical City. We included 63 children (37 boys and 26 girls) with low-grade gliomas treated at our center between January 2015 and December 2019. The median age at diagnosis was 7 years (range, 0.5–18 years). There were 40 patients with low-grade astrocytoma, 19 with low-grade oligodendroglioma, 2 with low-grade ganglioglioma, and 2 with low-grade ependymoma. The most common presenting symptom was progressive neurological deficit (86%). The most common imaging findings were mass effect (53%) and abnormal enhancement (54%). The most common genetic abnormalities were IDH1 (79%), ATRX (12%), and 1p/19q co-deletion (11%). The most common therapeutic approach was surgery followed by radiotherapy (56%). The 5-year overall survival rate was 82%, and the 5-year progression-free survival rate was 71%. The most common adverse events were mucositis (42.9%), skin rash, and paronychia (both 28.6%). Three patients required dose reduction and/or intermittent dose interruption. CONCLUSION: Our data supports the use of trametinib for both upfront and relapsed/refractory pediatric low grade gliomas with acceptable toxicity.
LOW-GRADE GLIOMA ASSOCIATION: A CASE REPORT

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BACKGROUND: Pilomyxoid astrocytoma (PMA) is a glial tumor that occurs predominantly in the hypothalamus-chiasmatic region and rarely in spinal cord. It has similar features as pilocytic astrocytomas, with some distinct histological characteristics and worse prognosis. The 2007 WHO recognized PMA as a Grade II glioma due to its aggressive behavior and dissemination tendency, but according to 2016 version grading of the pilomyxoid variant is under research. Here we report a case with a rare location, aggressive behavior and rapid progression. CASE PRESENTATION: A 7-year-old boy presented with headache, nausea, vomiting, and vomiting revealed an intramedullary tumor extending from C2 to C6 with hydrocephalus. A ventriculo-peritoneal shunt and complete surgical resection were performed with significant improvement in the patient’s condition. The patient received 6 months craniospinal irradiation 33.2 Gy with boosts to tumor bed and metastatic sites 49.6 GY and 54 Gy respectively. 11 months later tumor progression was revealed with new metastatic lesions in the bones. Patient received 6 cycles of chemotherapy with TMZ and Avastin, but continued to suffer disease progression on therapy and he succumbed to his disease at 24 months from diagnosis. CONCLUSION: Given the rarity of documented patients with spinal pilomyxoid astrocytoma with rapid progression, as well as the lack of certain WHO classification and treatment guidelines, this case report might be useful for development of more effective treatment strategies.

LOW-GRADE GLIOMA ASSOCIATION: A CASE REPORT

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BACKGROUND: MAPK pathway is the hallmark of pediatric low grade gliomas (pLGs); hyperactivation of mTOR (mammalian target of rapamycin) might be a suitable biomarker for therapeutic response. We investigated the feasibility of Everolimus in a pediatric glioma cell line panel. Cultured primary glioma cells were treated by pLGs. METHODS: Patients 1 to 18 years old, diagnosed with pLG, with a positive tumor biopsy for mTOR/phospho-mTOR and radioactive / or clinical disease progression, treated at Bambino Gesu Children’s Hospital in Rome were evaluated. Tumor DNA methylation analysis was performed in 10 cases. Exclusion criteria included: Tuberous sclerosis patients, Sub Ependymal Giant Astrocytoma. Everolimus was administered orally at a dose of 2.5 mg or 5 mg daily based on body weight. Patients were evaluated with brain MRI every 4, 8, and 12 months after treatment start and every six months thereafter. RESULTS: 16 patients were enrolled from September 2014 and 2019. The median age was 7.5 years old. All patients had at least one adverse event. Events rated as severe (grade 3/4) were reported in 6 patients. Stomatitis was the most frequent adverse event. One patient discontinued treatment due to grade 4 toxicity (ulcerative stomatitis and fatigue). The median duration of treatment was 21 months (4-57 months). Brain MRI evaluations have showed disease stability in 11 patients, partial response in 2 patients and disease progression in 3 patients. CONCLUSIONS: Everolimus has proven to be well tolerated and effective treatment in terms of disease stability in patients with pLGs. It’s also an excellent example of chemo-free personalized approach.

LOW-GRADE GLIOMA ASSOCIATION: A CASE REPORT

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BACKGROUND: MAPK pathway is the hallmark of pediatric low grade gliomas (pLGs); hyperactivation of mTOR (mammalian target of rapamycin) might be a suitable biomarker for therapeutic response. We investigated the feasibility of Everolimus in a pediatric glioma cell line panel. Cultured primary glioma cells were treated by pLGs. METHODS: Patients 1 to 18 years old, diagnosed with pLG, with a positive tumor biopsy for mTOR/phospho-mTOR and radioactive / or clinical disease progression, treated at Bambino Gesu Children’s Hospital in Rome were evaluated. Tumor DNA methylation analysis was performed in 10 cases. Exclusion criteria included: Tuberous sclerosis patients, Sub Ependymal Giant Astrocytoma. Everolimus was administered orally at a dose of 2.5 mg or 5 mg daily based on body weight. Patients were evaluated with brain MRI every 4, 8, and 12 months after treatment start and every six months thereafter. RESULTS: 16 patients were enrolled from September 2014 and 2019. The median age was 7.5 years old. All patients had at least one adverse event. Events rated as severe (grade 3/4) were reported in 6 patients. Stomatitis was the most frequent adverse event. One patient discontinued treatment due to grade 4 toxicity (ulcerative stomatitis and fatigue). The median duration of treatment was 21 months (4-57 months). Brain MRI evaluations have showed disease stability in 11 patients, partial response in 2 patients and disease progression in 3 patients. CONCLUSIONS: Everolimus has proven to be well tolerated and effective treatment in terms of disease stability in patients with pLGs. It’s also an excellent example of chemo-free personalized approach.