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=) or the combination therapy(n=). 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 study revealed the incidence of severe adverse events in two patients with BRAF targeted therapy. Due to the potential life-long use of targeted therapy, it is important to follow guidelines of adverse event monitoring and to develop a prevention and management strategy for severe adverse events.

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. METHODS: 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 a concurrent PTPN11 mutation) and 2 were positive for the 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 PTPN11 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 IDH-1 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 those <21 years (54%), while the prevalence of higher grade tumors increased with age. Interestingly, only 38% harbor IDH-1 mutations while 23% harbor pediatric mutations, including 8% with BRAF p.V600E, and 4% with *KIAA1549:BRAF* fusion. The median age for IDH-1 mutation is 32 years, with highest frequency in WHO grade II and III 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 fusion, p.V600E and IDH-1 p.R132H were 81%, 78% and 26% respectively. No survivors were observed in H3 p.K27M and p.G34R gliomas (p<0.0001). CONCLUSIONS: Gliomas in AYA overlap pediatric and adult classification and exhibit enrichment for pediatric alterations. As 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-induced senescence (OIS) initiated and sustained by senescence-associated secretory phenotype (SASP) factors. OIS and SASP in PA are thought to be driven by aberrations of the mitogen-activated protein kinase (MAPK) pathway (e.g. KIAA1549:BRAF fusion, $BRAF^{V600E}$ mutation, for the most common MAPK alterations occuring in PA), leading to its sustained activation. The MAPK pathway cascade is activated in a sequential manner: 1) ERK activation, which phosphorylates downstream partners in both cytoplasm and nucleus. 2) ERK-mediated induction of immediate early genes encoding transcription factors. 3) Induction of MAPK target genes expression. 4) Activation of downstream pathways. Our aim is to unravel the molecular partners involved at each level of the sustained MAPK pathway activation in pLGG with different genetic backgrounds (KIAA1549:BRAF fusion and $BRAF^{V600E}$ mutation), and leading to the induction of OIS and SASP factors expression. pLGG cell lines DKFZ-BT66 (KIAA1549:BRAF) and BT-40 ($BRAF^{V600E}$) were treated with the MEK inhibitor trametinib at key time points, and gene expression profile analysis was performed, allowing transcriptome analysis at each step of the MAPK cascade. This will be combined with a whole proteomic and phospho-proteomic analysis. Combination of the transcriptome and proteome data layers will allow the identification of a) downstream targetable partners activated by the MAPK pathway involved in PA senescence, b) new putative targets that might bring benefit in combination with MAPK inhibitors.

LGG-15. PEDIATRIC LOW-GRADE GLIOMAS IN SAUDI ARABIA: RETROSPECTIVE ANALYSIS OF CHILDREN WITH LOW-GRADE GLIOMAS TREATED IN KING FAHAD MEDICAL CITY KFMC-SINGLE INSTITUTIONAL EXPERIENCE

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