enriched for WHO grade I histology (88% versus 66%, p<0.0001), infrequently progressed (27% versus 46%, p<0.0001), and rarely resulted in death (3 versus 13%, p<0.0001) as compared to SNV-driven tumors. These included the rarest molecular drivers of pLGG, for which we now have the clinicopathologic features of including MYB, MYBL1, FGFR2 fusions, FGFR1-TACC1, FGFR1 SNVs, IDH1 p.R132H, and H3.3 p.K27M. Utilizing this information, we suggest novel risk categories of pLGG that effectively predicted patient outcome. Low-risk tumors progressed infrequently and rarely succumbed to their disease (10-year PFS of 71% and OS of 98%). Intermediate-risk pLGG had a 10-year PFS and OS of 35% and 90%, respectively. High risk pLGG almost invariably progressed (10-year PFS of 0%) and these patients often succumbed to their disease (10-year OS of 41%). These data highlight the biological and clinical differences between pLGG subtypes and offers molecular based risk stratification to these cancers.

LGG-51. BRAF ALTERATIONS IN PEDIATRIC LOW-GRADE GLIOMAS: RESULTS FROM A BRAZILIAN COHORT

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BACKGROUND: Pediatric low grade gliomas (PLGG) are the most common central nervous system neoplasms in children. These are driven almost exclusively by alterations in the RAS/MAPK pathway. Specifically, alterations in the BRAF gene have emerged as an important target for therapy. This study aimed to identify the frequency of BRAF alterations in a Brazilian cohort of PLGGs. RESULTS: Forty-one patients diagnosed between 2001 and 2017 had enough FFPE tissue available for analysis. Real-time PCR test (n=35) was used to assess for BRAFV600E mutations, while BRAF fusions were detected by break-apart fluorescence *in situ* hybridization (n=30). The histologic distribution was as follows: 73% pilocytic astrocytoma, 12% ganglioglioma, 3% diffuse astrocytoma, 5% pleomorphic xanthoastrocytomas (PXA) and 7% NOS (n = 41). BRAF fusions were present in 21 patients (51%): 17 pilocytic astrocytomas, 2 xanthoastrocytoma, 1 pilomyxoid astrocytoma and 1 diffuse astrocytoma. BRAFV600E was detected in 4 cases (10%): 2 pilocytic astrocytomas, 1 ganglioglioma and 1 PXA. As expected, BRAF translocations were more frequent in pilocytic astrocytomas (p<0.001). From 22 patients treated in our institution, 59% were male with a mean age of 9.7 years, 50% occurred in the posterior fossa and 77% treated by surgery only. One patient relapsed and died from disease (BRAF V600E positive) (follow-up median=44.7 months). These are the first results using a CLIA method showing the frequency of BRAF abnormalities in a Brazilian population. Although preliminary, BRAF alterations are present in 61% of the cases emphasizing the importance of incorporating this analysis in the current work-up guidelines.

LGG-52. BINIMETINIB IN CHILDREN WITH PROGRESSIVE OR RECURRENT LOW-GRADE GLIOMA NOT ASSOCIATED WITH NEUROFIBROMATOSIS TYPE 1: INITIAL RESULTS FROM A MULTI-INSTITUTIONAL PHASE II STUDY

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BACKGROUND: RAS/RAF/MEK/ERK pathway activation is the primary driver for most pediatric low-grade gliomas (LGG). Binimetinib is an orally bioavailable MEK1/2 inhibitor found to have significant central nervous system penetration in a preclinical model. OBJECTIVE: The primary objective of this multi-institutional open-label phase II study was to assess preliminary efficacy of binimetinib in progressive pediatric LGG. The study included strata for both neurofibromatosis type I (NF1) and non-NF1 associated tumors, as well as a target validation (surgical) stratum. NF1 and surgical strata remain open to enrollment and will be reported separately. METHODS: Children aged 1–18 years with previously treated recurrent or progressive LGG were eligible. The dose of binimetinib was 32 mg/m^2/dose twice daily. Partial and minor responses were defined, respectively, as 50% and 25% decrease in maximal two-dimensional measurements. RESULTS: Fifty-seven eligible patients without NF1, median age 8 years, were enrolled and began treatment; 26 were female; 28 had documented KIAA1549-BRAF fusion. Eleven patients discontinued drug in the first year due to toxicity, and an additional 27 required dose reduction. The most common drug-attributable grade 3 toxicities included creatine kinase elevation (n=9 patients), rash (n=8), and truncal weakness (n=8). Truncal weakness improved or resolved with dose reduction or cessation. Grade 4 toxicities included creatine kinase elevation (n=2) and transient colitis (n=1). Of 44 patients with preliminary response data available, 22 (50%) showed a minor (n=7) or partial (n=15) response. CONCLUSION: Binimetinib is active, with manageable toxicities, in children without NF1 with progressive LGG.

LGG-53. PNOC001 (NCT01734512): A PHASE II STUDY OF EVEROLIMUS FOR RECURRENT OR PROGRESSIVE PEDIATRIC LOW-GRADE GLIOMAS (PLGG)

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OBJECTIVE: To estimate the 6-month Progression Free Survival (PFS6) associated with everolimus for progressive/recurrent pLGGs and to determine if activated PI3K/Akt/mTOR pathway as measured by positive phosphorylated-ribosomal protein S6 (p-RPS6) status was associated with response. METHOD: Patients 3–21 years of age with recurrent or progressive pLGG were enrolled. Everolimus was administered orally at 5 mg/m^2 daily. Tissue availability for molecular analysis was mandatory. Immunohistochemistry (IHC) for p-RPS6 was performed centrally. An adaptive Simon two-stage design was employed based on p-RPS6 status. Based on results of the first stage, enrollment in the second stage was either limited to pathway activated patients or open to all subjects. RESULTS: From December 2012 to July 2019 a total of 65 subjects enrolled [median age 9 years (range 3–19); 43% female]. As of December 15, 2019 median number of treatment cycle is 8 (range 1–24); 7 patients remain on treatment. Toxicity profile is similar to published reports with rash and elevated lipid profiles as most common adverse events. PFS6 for the entire cohort is 63%; PFS6 is 64% for the activated and 61% for the non-activated patients. Central imaging review (n=52) revealed 1 partial response, 1 complete response, 33 stable disease, and 17 progressive disease at the end of study treatment. Initial molecular analysis identified BRAF alterations in 35/65 patients. CONCLUSION: Everolimus is well tolerated and active in a subset of pLGGs. Ongoing analyses will assess predictive biomarkers of response and will be reported at the meeting.

LGG-54. DETECTION OF THE KIAA1549-BRAF FUSION GENE IN CELLS FORMING MICROVASCULAR PROLIFERATIONS IN PILOCYTIC ASTROCYTOMA

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Microvascular proliferation (MVP), an aberrant vascular structure is a histopathological hallmark of glioblastoma multiforme (GBM). Although MVP tends to be associated with high-grade glioma, it has also been detected in WHO grade I pilocytic astrocytoma (PA). However, little is known about the mechanism underlying its formation. Using TP53 point mutations as a marker for tumor-derived cells, we earlier reported that MVP was partially converted from tumor cells via mesenchymal transition. In the current study we used the KIAA1549-BRAF fusion gene as a marker to assess whether MVPs in PA contained tumor-derived cells and/or phenotypically