

distinct tumor cells expressing vascular markers. Samples from three PA patients harbored the KIAA1549 exon 15, BRAF exon 9 fusion gene. In two patient samples with abundant MVP, RT-PCR assay detected strong bands arising from the KIAA1549-BRAF fusion gene in both tumor cells and cellular components of MVP. Digital PCR showed that vis-à-vis tumor tissue, its relative expression in cellular components of MVP was 42% in one- and 76% in another sample. FISH revealed amplified signals in both tumor cells and cellular components of MVP indicative of tandem duplication. Our findings suggest that in patients with PA, some cellular components of MVP contained tumor derived cell and/or phenotypically distinct tumor cells expressing vascular markers.

LGG-55. OUTCOME OF BRAF V600E PEDIATRIC GLIOMAS TREATED WITH TARGETED BRAF INHIBITION

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Children with pediatric gliomas harboring BRAF V600E mutation have a poor outcome with current chemoradiation strategies. Our aim was to study the role of targeted BRAF inhibition in these tumors. We collected clinical, imaging, molecular and outcome information from BRAF V600E glioma patients treated with BRAFi across 29 centers from multiple countries. Sixty-seven patients were treated with BRAFi (56 pediatric low grade gliomas, PLGG and 11 pediatric high grade gliomas, PHGG) for up to 5.6 years. Objective responses were observed in 80% of PLGGs compared to 28% with conventional chemotherapy (p<0.001). These responses were rapid (median, 4 months), and sustained in 86% of tumors up to 5 years while on therapy. PLGG which discontinued BRAFi, 76.5% (13/17) progressed rapidly after discontinuation (median 2.3 months). However, upon re-challenge with BRAFi therapy, 90% achieved an objective response. Poor prognostic factors to conventional therapies, such as concomitant homozygous deletion of *CDKN2A*, were not associated with a lack of response to BRAFi. In contrast, only 36% of PHGG responded to BRAFi with all but one tumor progressing within 18 months. In PLGG, responses translated to 3-year progression-free survival of 49.6% (95%CI, 35.3% to 69.5%) vs

29.8% (95% CI, 20% to 44.4%) for BRAFi vs chemotherapy respectively (p=0.02). The use of BRAFi results in robust and durable responses while on therapy in BRAF V600E PLGG. Prospective studies are required to determine long-term survival and functional outcomes with BRAFi therapy in childhood gliomas.

LGG-56. INFANTILE HEMISPHERIC BRAIN TUMOR WITH A GPCR-ROS1 FUSION GENE: A CASE REPORT

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INTRODUCTION: Infantile hemispheric gliomas with *ROS1* fusion genes have been reported to have a relatively poor prognosis. Treatment using a *ROS1* inhibitor is expected to generate less toxicity and effective for brain tumors with *ROS1* fusion genes. **CASE PRESENTATION:** A one-month-old female presented with a seizure, and a large hypervascular mass in the right hemisphere was found on MRI. The tumor was not biopsied over concerns of an increased risk for bleeding. The mass was clinically diagnosed as an atypical teratoid rhabdoid tumor. She received neoadjuvant chemotherapy using the modified EU-RHAB protocol. The tumor gradually decreased to 70% of its original size with a reduction of vascularity. A near-total resection (> 95%) was performed at eight months of age. Pathological examination revealed the unusual histology with immunostaining positive for INI-1, GFAP, synaptophysin, neurofilament, and slightly positive for NeuN. MIB-1 labeling index was 6%. The pathological diagnosis was a glioneuronal tumor with desmoplastic infantile ganglioglioma-like features, suggestive of low grade. She received adjuvant chemotherapy with carboplatin and vincristine, which is the standard treatment for low-grade gliomas, and achieved a partial response. The *GPCR-ROS1* fusion gene was detected in the tumor by FoundationOne® CDx. **CONCLUSION:** Chemotherapy may effectively reduce the size of an infant's brain tumor which is initially considered to be inoperable. A gene profile should be performed as soon as possible in order to direct appropriate management.

LGG-57. SIGNALLING MECHANISMS IN PAEDIATRIC LOW-GRADE GLIOMA

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Paediatric low-grade gliomas (pLGGs) constitute the largest group of childhood CNS tumours. They often cause significant disability and morbidity, despite their indolent growth and the good survival rate of patients. The most common genetic alterations in these tumours, *KIAA1549:BRAF* fusion and *BRAFV600E* mutation, lead to abnormal activation of MAPK signalling. The central role of this pathway in pLGG development is emphasized by the occasional presence of other MAPK-activating alterations such as RTK mutations. It is not known how these different aberrations can induce the variety of clinical phenotypes seen in pLGG. Here, we compared pilocytic astrocytomas (PAs) containing the *KIAA1549:BRAF* fusion with glioneuronal tumours (GNTs) containing the *BRAFV600E* mutation, to identify differentially activated downstream targets of the MAPK pathway. Liquid chromatography tandem mass spectrometry (LC-MS/MS) was used as a multi-proteomic approach. Kinase Set Enrichment Analysis (KSEA) using PhosphositePlus and NetworkIN was used to determine relative enrichment of kinase activity in the tumours compared to healthy control brain tissue. Significant similarities and differences were found in the two tumour types. For example, more robust MAPK activation was found in the GNTs than in PAs. However, while PI3K/AKT/mTOR signalling was active in both PAs and GNTs, there was statistically higher activation in the PAs. In both tumour types, there was significant reduction in casein kinase 2 activity, which likely affects nuclear translocation of ERK and, in turn, alters the range of its phosphorylated substrates. We will present these data together with transcriptomics to further characterise the downstream targets of these genetic alterations.