eral ophthalmologic side effects, including MEK inhibitor-associated retinopathy (MEKAR), also termed central serous-like retinopathy. MEKAR is defined as accumulation of subretinal fluid. It occurs in up to 90% of adults on MEK inhibitors, usually causing minimal to no symptoms, and typically resolving without MEK inhibitor dose adjustment. We report a case of MEKAR in a 15 year old boy with an optic pathway pilocytic astrocytoma with duplication of BRAF (7q34). Baseline ophthalmic exam showed 20/20 vision in his right eye with loss of the temporal hemifield and no light perception vision in the left eye. Nine months into treatment with Selumetinib his ophthalmologic exam and optical coherence tomography (OCT) showed asymptomatic bilateral subretinal fluid. Selumetinib was held for 2 weeks resulting in resolution of the subretinal fluid. Selumetib was resumed at the prior dose and MEKAR recurred 2 weeks later but then permanently resolved 4 weeks later despite remaining on Selumetib. Review of the literature discovered a single publication of 2 pediatric patients with optic pathway glioma who developed MEKAR around 6-7 months after initiating Selumetinib, which resolved after stopping Selumetinib. One patient was symptomatic and despite resolution of symptoms, Selumetinib was not resumed. The other patient was asymptomatic and resumed Selumetib, but redeveloped MEKAR 8 months after restarting Selumetinib. Based on adult experience and the limited pediatric experience outlined above, we recommend pediatric patients with asymptomatic and mild-moderate symptomatic MEKAR undergo close monitoring without Selumetinib dose interruption or modification unless symptoms progress.

LGG-64. A PHASE II STUDY OF PEGYLATED INTERFERON IN CHILDREN WITH RECURRENT OR REFRACTORY AND RADIOGRAPHICALLY OR CLINICALLY PROGRESSIVE JUVENILE PILOCYTIC ASTROCYTOMAS AND OPTIC PATHWAY GLIOMAS (NCT02343224)

Dolly Aguilera[1], Claire Mazewski[1], Anna Janss[1], Tobey MAcDonald[1], Adam Goldman[1], Tracy Leong[2], Robert Craig Castellino[1]; [1]Children's Health Care of Atlanta, Emory University School of Medicine, Atlanta, GA, USA. [2]Emory University, Atlanta, GA, USA

Unresectable Juvenile Pilocytic Astrocytomas (JPA) and Optic Pathway gliomas (OPG) are chronic diseases that can have solid +/- cystic components. We wanted to evaluate the objective response to pegylated interferon Alpha2B in this group of patients in a prospective single arm Phase II clinical trial. Eligibility criteria: age 3 -25 years, patients with neurofibromatosis (NF) were eligible, evidence of measurable disease in MRI, no limitation in the number of prior therapies including chemotherapy and radiation. Exclusion criteria: prior pegylated interferon exposure, less than 2 years from radiation, active autoimmune disease. Subjects enrolled received pegylated interferon 1 mcg/kg/dose SQ weekly, to a max dose of 150mcg/dose in 28 day cycles for up to 2 years. The study design is a Simon two stage design. If no complete or partial responses among the first 9 patients, the study will terminate. Nine subjects enrolled: 4 females, 5 males, median age of 11years, 6 Caucasians, 3 African Americans. Two subjects with NF. Molecular findings KIAA-BRAF fusion (6), V600E mutation (1), CDK2A loss (1). Location: brain (7), brain and spine (2). We enrolled a heavily pre-treated population, patients with prior radiation (1), nine with prior chemotherapy, the average number of regimens 4 (range 2-6). No complete responses or partial responses were seen. Two patients with prolonged stable disease 75+months and 66+ months. At 12 and 24 month EFS 76.2% (95%CI52.1-100%). Median EFS has not been reached. The 12 and 24 months survival estimate 75% (95% CI 50.3-100%), median survival has not been reached. Side effects as expected mostly grade 1-2. No grade 4 event related to pegylated interferon were seen. This is the first report of pegylated interferon in OPG and JPA, two patients with prolonged stable disease suggesting that pegylated interferon can offer potential benefit in this population and additional studies are important.

MEDULLOBLASTOMA

MEDB-01. MANAGEMENT OF THE RISK OF MEDULLOBLASTOMA ASSOCIATED TO FAMILIAL ADENOMATOUS POLYPOSIS AND DYSREGULATED WNT SIGNALOSOME

Balkiss Abdelmoula, Fatma Abid, Amir Karra, Sonda Kammoun, Samir Aloulou, Nouha Bouayed Abdelmoula; Genomics of Signalopathies at the service of Medicine, Sfax, Tunisia

APC is the key gene of the familial adenomatous polyposis (FAP). This tumor suppressor gene functions by negatively regulating the β-catenin protein and the majority of APC mutations disrupt the β-catenin degradation complex signalosome leading to the activation of the canonical Wnt pathway. Pathogenic APC mutations were reported in association to medulloblastoma. In this study, we report rare mutations of the APC gene detected in Tunisian families from the governorate of Sfax presenting clinically with various digestive and extra-digestive manifestations. Our goal was to assess the oncogenic risks encountered by our pediatric carriers to offer an accurate genetic counselling, particularly at the neurologic level. Molecular investigation of all members of two families was conducted, using bidirectional sequencing of all 15 exons of the APC gene. A phenotype-genotype correlation was conducted to elucidate the mutational pathophysiological mechanism. Two rare mutations were revealed in our familial study. The first mutation was located at exon 13 and was a missense mutation at codon 1690. The second mutation was a deletion identified at codon 4652 in exon 15. The mutations resulted both in truncated gene products. Clinical manifestations closely depending on the position of the mutation were respectively colic polyposis for the first mutation and soft tissue fibromatous tumors for the second. The localization of the APC mutations allows better targeting of surveillance for clinical manifestations that may be included in FAP. Mutations that remove the Axin-binding sites, as is the case for the first mutation, lead to severe clinical pictures whereas mutations that retain one or two of the Axin binding sites are associated with other features such as desmoid tumors. The risk of the Wnt- medulloblastoma subtype, higher among patients with FAP should be considered with a more awareness of signs and symptoms related to CNS tumors in the FAP context.

MEDB-02. THE IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF CIRCULAR RNA CIRC_63706 IN SONIC HEDGEHOG MEDULLOBLASTOMAS

Rudramani Pokhrel[1,2], Keisuke Katsushima[1,2], Stacie Stapleton[2], George Jallo[2], Eric Raabe[1,3], Charles G. Eberhart[1,3], Ranjan J. Perera[1,2]; [1]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, School of Medicine, Johns Hopkins University, Baltimore, MD, USA. [2]Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA. [3]Department of Pathology, School of Medicine, Johns Hopkins University, Baltimore, MD, USA

Circular RNAs (circRNAs) are increasingly recognized as stable and specific biomarkers and therapeutic targets in many cancers, but little is known about their function, subtype specificity, and biomarker potential in medulloblastomas. Medulloblastoma is a central nervous system tumor that predominantly affects children and always requires aggressive therapy. Understanding and identifying novel disease-related molecular mechanisms and pathways are essential for developing optimal and novel therapies. To identify medulloblastoma subgroup-specific circRNAs, we subjected RNA-seq data from 175 clinical medulloblastoma samples representing the four subgroups to a statistical and machine learning (random forest classification) pipeline. Circular RNA circ_63706 expression was specific to the sonic hedgehog (SSH) group, which was confirmed through *in situ* hybridization analysis of clinical tissue samples. Functional characterization of circ_63706 by siRNAs and shRNAs demonstrated that cell proliferation, invasion, and apoptosis are perturbed in circ_63706 cells and inhibited *in vivo* tumor growth. These novel medulloblastoma-specific circular RNAs are emerging as important oncogenes that not only provide valuable mechanistic insights into how medulloblastomas develop but also how they can be used as biomarkers and therapeutic targets. These results pave the way for the specific identification and personalized treatment of different medulloblastoma subgroups.

MEDB-03. MEDULLOBLASTOMA CEREBROSPINAL FLUID REVEALS HYPOXIC INDICATORS (METABOLITES AND LIPIDS) AND CANCER-SPECIFIC RNAS

Bongyong Lee[1,2], Iqbal Mohamad[3], Rudramani Pokhrel[1,2], Rabi Murad[4], Menglang Yuan[1,2], Stacie Stapleton[2], Chetan Bettegowda[1,5], George Jallo[2], Charles G. Eberhart[1,6], Timothy Garrett[3], Ranjan J. Perera[1,2]; [1]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, School of Medicine, Johns Hopkins University, Baltimore, MD, USA. [2]Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA. [33]Department Pathology, Immunology and Laboratory Medicine, University of Florida, College of Medicine, Gainesville, FL, USA. [4]Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA, USA. [5]Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA. [6]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Medulloblastoma (MB) is the most common malignant brain tumor in children. There remains an unmet need for diagnostics to sensitively detect the disease, particularly recurrences. Cerebrospinal fluid (CSF) provides a window into the central nervous system, and liquid biopsy of CSF could provide a relatively non-invasive means for disease diagnosis. There has yet to be an integrated analysis of the transcriptomic, metabolomic, and lipidomic changes occurring in the CSF of children with MB. CSF samples from patients with (n=40) or without (n=11; no cancer) MB were subjected