Gaslini, Genoa, Italy. [3]Pharmacy, IRCCS Istituto Giannina Gaslini, Genoa, Genoa, Italy. [4]Neurosurgery Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy

BRAF inhibitors (iBRAF) are under investigations in ongoing clinical trials for pediatric brain tumor treatment. Preliminary data regarding the pediatric population report pyrexia, hematological, dermatological, cardiac, and ophthalmic toxicities among the most common adverse events. Acute kidney injury (AKI), mainly due to tubular interstitial injury, has been reported in the adult population. With our study we want to contribute to a more comprehensive knowledge of the short- and long-term nephrological adverse effects of iBRAF in a pediatric population. We collected and reviewed clinical and laboratory data of all patients treated with iBRAF for pediatric central nervous system tumors at our Institution and available for publication. AKI was monitored through serial creatinine measurements, kidney function with estimated glomerular filtration rate (eGFR) and kidney injury with creatinuria/proteinuria ratio. Tubular injury was evaluated with fractional excretion of sodium, potassium and magnesium and with glycosuria. Moreover, urine was examined to detect presence and morphology of erythrocytes. Eight patients were identified, 3 females; median age at treatment start was 9 years (range 2,75 – 18,75). Six patients with BRAFV600E–mutated pediatric Low-Grade Glioma were treated with Vemurafenib, 1 patient with BRAFV600E-mutated pediatric High-Grade Glioma was treated with Vemurafenib and 1 patient with BRAFV600E-mutated Langerhans Cell Histiocytoses was treated with Dabrafenib. Seven patients were considered for analysis. After a median follow up of 3,83 years (range 2,25 – 6,58) no AKI was reported and all patients but two retained normal eGFR at last follow up. No tubular and glomerular injury laboratory findings were detected, and erythrocytes in the urine resulted always below the upper limit of normality. CONCLUSIONS: iBRAF were not associated with AKI and tubular injury. Nevertheless, some data, namely significative decrease of eGFR in two out of seven patients, warrants further investigations.

### LGG-35. DYSLIPIDEMIA IN CHILDREN TREATED WITH BRAF INHIBITORS FOR BRAIN TUMOR, A NEW SIDE EFFECT? A SINGLE CENTER RETROSPECTIVE STUDY

Marco Crocco[1,2], Antonio Verrico[1], Claudia Milanaccio[1], Gianluca Piccolo[1,2], Gabriele Gaggero[3], Patrizia De Marco[4], Valentina Iurilli[5], Sonia Di Profio[6], Maria Grazia Calevo[7], Emilio Casalini[8,2], Natascia Di Iorgi[8,2]; [1]Neuroncology Unit, IRCCS Istituto Giannina Gaslini, Genova, Italy. [2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Genova, Italy. [3]Department of Clinical Pathology, IRCCS Ospedale Policlinico San Martino, Genova, Italy. [4]UOC Genetica Medica, IRCCS Istituto Giannina Gaslini, Genova, Italy. [5]Pharmacy Unit, IRCCS Istituto Giannina Gaslini, Genova, Italy. [6]Clinical Psychology, IRCCS Istituto Giannina Gaslini, Genova, Italy. [7]Epidemiology and Biostatistics Unit, IRCCS Istituto Giannina Gaslini, Genova, Italy. [8]Department of Pediatrics, IRCCS Istituto Giannina Gaslini, Genova, Italy

The targeted therapies for brain tumors are innovative and promising oncological treatments and as a result their use has expanded widely. BRAF inhibitors (BRAFi) in recent years have played a central role in disease control of unresectable BRAF-mutated pediatric low-grade gliomas (LGG). Understanding the side effects of these drugs is crucial for clinical practice. The aim of the study was to investigate retrospectively the acute and long-term effects of vemurafenib on lipid metabolism in children treated for an LGG. Children (n=6) treated with vemurafenib at the mean age of 8.41±6.1 exhibited early alterations in plasma lipid profile as demonstrated after 1 month (n=4) by high plasma levels of Low-Density Lipoprotein (LDL 139.5±51.5,mg/dL), Total Cholesterol (TC 221.5±42.1,mg/dL) and Triglycerides (TG 107.8±44.4,mg/dL). Despite dietary recommendations, dyslipidemia persisted 3 months later (LDL 148.8±40.2,mg/dL; TC 238±36.5,mg/dL; TG 115±45.6,mg/dL; n=4) and at long distance follow-up (38±23,months) after treatment with vemurafenib: LDL 139.2±49.1,mg/dL; TC 216.5±38.4,mg/dL; TG 129.7±83.4 mg/dL. This potential side effect suddenly resolved itself in the only patient in which a change of therapy was made (to the combination of dabrafenib and trametinib). BMI was compatible with overweight/obesity at baseline (mean BMI-SDS 0.9±1.8) in 2 patient and normal in 4 patients: during follow-up BMI remained stable in 5 patients and increased in 1 patient. Our findings highlight that Vemurafenib could be associated with an increased risk of dyslipidemia independently of weight. This risk should be anticipated by the identification of high-risk patients and managed by close monitoring of metabolic parameters during routinely follow-up. The association of dabrafenib with trametinib seem not be associated to dyslipidemia, yet more data are needed to explore the hypothesis about the possible role to reduce the risk of dyslipidemia.

### LGG-36. ANALYSIS OF BRAF-RELATED MUTATIONS IN PEDIATRIC LOW-GRADE GLIOMA

Shaoqun Li, Mingyao Lai, Linbo Cai; Guangdong Sanjiu Brain Hospital, Guangzhou, Guangdong, China

BACKGROUND: Most pediatric low-grade gliomas (pLGGs) are driven by a single genetic event resulting in up-regulation of the RAS/MAPK pathway. BRAF-related mutations are the most freauent molecular alteration in the pathway. To explore BRAF-related mutations in pediatric low-grade glioma is helpful for clinical practice. METHODS: In this study, patients with low-grade glioma aged ≤18 years in Guangdong Sanjiu Brain Hospital were enrolled. All patients accepted the tests of BRAF-related mutations with tumor tissue by next-generation sequencing (NGS). Results: A total of 26 patients diagnosed low-grade glioma and underwent NGS detection were included in this study. The male to female ratio was 6:7, and the median age was 9.5 years. 8 patients had tumors located in the cerebral hemisphere, 6 in the third or fourth ventricle, 5 in the cerebellum, 4 in the optic pathway, and 3 in the brain stem. A total of 14 patients took BRAF-related mutations, such as BRAF-KIAA1549 fusion, BRAF p.V600E mutation and other fusion. BRAF-KIAA1549 fusion was detected in 7 patients with pilocytic astrocytoma or pilomyxoid astrocytoma. BRAF p.V600E mutation was detected in 6 patients, two of whom were pleomorphic xanthoastrocytoma. A rare genetic fusion, BCAS1-BRAF fusion, was detected in 1 patient who had brain stem ganglioglioma. Among the 26 patients, 2 patients without BRAF-related mutations had typical multiple cafe-au-lait macules and were diagnosed as NF1-pLGG. These patients were treated with surgery, radiation, chemotherapy and targeted therapy. Only 2 patients received targeted therapy by Trametinib, Vimofinib and Everolimus after progression of the tumor. However, due to the severity of the disease, they eventually died. CONCLUSIONS: More than half of pLGG patients have BRAF-related mutations, which have the opportunity for targeted therapy. However, the optimal timing of targeted therapy still needs further exploration.

### LGG-37. LONG-TERM OUTCOME, VISUAL MORBIDITY AND PROGNOSTIC FACTORS IN INFANTS AND YOUNG CHILDREN WITH OPTIC PATHWAY GLIOMA FROM THE GREAT ORMOND STREET HOSPITAL (GOSH) LGG - COHORT

Stefania Picariello[1], Brownen Walters[2], Richard Bowman[2], Olga Slater[3], Mette Jorgensen[3], Christine Dahl[3], Patricia O'Hare[4,3], Helen A. Spoudeas[5,6], Hong-Wei Gan[5], Kristian Aquilina[7], Yen Ch'in Chang[8], Felice D'Arco[9], Darren Hargrave[3], Enrico Opocher[10,3]; [1]Department of Paediatric Oncology, Napoli, Italy. [2]Ophthalmology Department, Great Ormond Street Hospital, London, United Kingdom. [3]Paediatric Oncology, Great Ormond Street Hospital, London, United Kingdom. [4]Paediatric Oncology, Belfast, United Kingdom. [5]Endocrinology Department, Great Ormond Street Hospital, London, United Kingdom. [6]section of molecular basis of rare disease, University College University, London, United Kingdom. [7]Paediatric Neurosurgery, Great Ormond Street Hospital, London, United Kingdom. [8]Radiotherapy Dep. UCLH, London, United Kingdom. [9]Department of Radiology, Great Ormond Street Hospital, London, United Kingdom. [10]Paediatric Hematology, Oncology and Stem Cell Transplant Division, Padua University Hospital, Padua, Italy

INTRODUCTION: The treatment aim of childhood optic pathway glioma (OPG) is visual preservation. However, long-term outcomes and prognostic factors implicated remain largely unknown. METHODS: We undertook a retrospective study of infants and young children (IYC) ≤3 years with OPG and logMAR visual acuity (VA) at baseline/follow-up. We derived Overall- (OS), Progression-free (PFS), Radiotherapy-free (RTFS) and Visual event-free survival (vEFS) curves and analysed prognostic factors for visual deterioration and WHO defined blindness (>1.3 logMAR both eyes). RESULTS: Of 81 IYC-OPG (147 evaluable eyes) baseline vision was below 5%ile for age in 33 (41%) and 27 (33%) in one or both eyes respectively, within normal range in 21 (26%). After observation (11), chemotherapy (66) or RT (4), radiological progression occurred in 47 (58%), multiple times in 34.6% (range 2 - 8) and 10yr-PFS was 39.8%. Twenty had RT after 4.2 years from diagnosis (10yr-RTFS 72.4%) and 12% died (10yr-OS 89%). After 8.9 years VA was better/stable/ worse in 36%/32%/32% of subjects, with median time to visual event of 1.7 years (range 0.16 - 12) and 10yr-vEFS 41.3%. Final VA was reduced (>0.2 logMAR) in 23 (28.4%) and 43 (53.1%) in only one or both eyes respectively. Amongst those with unilateral impairment 13/23 affected eyes had no useful vision (light/no light perception). Amongst those with bilateral impairment best eye VA was > 1.0 log MAR in 22/43 (LP/NLP in 10). Infants < 1 year had significantly inferior 10-yrPFS (5.6%), post-chiasmatic involvement was associated with visual deterioration (HR 2.91, 95%CI=1.1- 7.7), and baseline bilateral abnormal for age vision predicted WHO blindness at follow-up (OR 17.9, 95%CI=3.2 – 101.1). CONCLUSIONS: Many IYC-OPG suffer multiple progressions with significant long-term visual morbidity. Predictive factors such as age, tumor location and baseline age-adjusted vision allow patients' selection for early sight rehabilitation and consideration for experimental strategies preventing visual loss.

### LGG-38. DOSE-DEPENDENT SEIZURE CONTROL FOR AN NF1 PATIENT TREATED VIA MEK-INHIBITION FOR OPTIC PATHWAY GLIOMA

Evan Cantor, Ashley Meyer, Andrea Ogle, Margaret Shatara, Andrew cluster, Mohamed S. Abdelbaki, Stephanie Morris, Judith Weisenberg, Nicole M. Brossier; Saint Louis Children's Hospital, St. Louis, MO, USA

BACKGROUND: Low-grade gliomas (LGG) are the most common solid tumor of childhood and can result in neurologic complications, including seizures, focal neurologic deficits, and learning difficulties. Molecularly tar-