LGG-29. USE OF BEVACIZUMAB IN PEDIATRIC LOW-GRADE GLIOMA: TEN-YEAR EXPERIENCE IN A SINGLE CENTER

Margarida Simão Rafael, Ofelia Cruz, Sara Perez-Jaume, Vicente Santa-María, Cinzia Lavarino, Hector Salvador, Jordi Muchart, Jose Hinojosa, Mariona Suñol, Andrés Morales; Hospital Sant Joan de Déu, Barcelona, Spain

PURPOSE: Pediatric low-grade gliomas (PLGG) have excellent overall survival but frequently need non-surgical therapy at diagnosis or after progression at unresectable sites such as the optic pathway. Chemotherapy side effects have led to the need for better-tolerated regimens with a sustained response. Bevacizumab, a humanized anti-VEGF monoclonal antibody has been used in monotherapy and/or in combination for these entities. Here we present our experience with its use in PLGG. METHODS: A retrospective, observational, single-institution study between 2008-2018 was performed, reporting the short-term outcomes of safety and efficacy of bevacizumab in progressive PLGG. RESULTS: Twenty-six patients with a median age at diagnosis of 3.32 years old [0.12-14.7] and the median age at the treatment of 8.11 years old [0.41-16.82] were included in the study. Nineteen had optic pathway gliomas and chiasmatic-hypothalamic gliomas (73.1%), 9 of them (47.4%) associated with neurofibromatosis type 1 (NF1). Fourteen non-NF1 tumors were molecularly studied, disclosing BRAF-KIAA1549 fusion transcript in 9 and BRAF V600E mutation in 2. Bevacizumab was administered in combination with other agent(s) in 16 of the 35 treatment courses. Responses were assessed at 3, 6, 12 months, and at the end of treatment. Progression-free survival at 12 months was 94%, and no severe adverse events were observed. CONCLUSIONS: In our series, Bevacizumab in PLGG showed short-term clinical efficacy with a favorable toxicity profile. Larger and long-term prospective studies may determine whether the response is conditioned upon different clinical or molecular features.

LGG-31. PEDIATRIC LOW-GRADE GLIOMAS WITH FGFR1 MUTATIONS AND SPONTANEOUS HEMORRHAGE: CASE SERIES

Stephani Campion[1], Ana E. Aguilar-Bonilla[1], Samer Elbabaa[2], Amy A. Smith[2]; [1]Orlando Health, Orlando, Fl, USA. [2]Orlando Health, Orlando, FL, USA

Pediatric low-grade gliomas (pLGG) are the most common pediatric CNS neoplasms. Thanks to the advent of molecular tumor diagnostics, we have begun exploring the clinical relevance of FGFR1 (c.1632C>A; p.N546K) mutations in the pLGG population. However, the risk of spontaneous hemorrhage in pLGG patients harboring FGFR1 mutations is even less understood. We present four pLGG cases with FGFR1 mutation and hemorrhagic episodes. Patient 1 presented with an intraventricular hemorrhage and leptomeningeal disease. Pathology was consistent with suprasellar pilocytic astrocytoma, FGFR1, and PTPN11 mutations. Initial therapy consisted of Carboplatin/Vinblastine per ADVL0515. The patient has had several recurrences, and treatment regimens have included ACNS0223, Everolimus, and A9952 regimen A. Patient 2 was diagnosed with an optic pathway glioma, and pathology confirmed FGFR1, MEK2, PTPN11, and NF1 splice site mutations. The patient also has a history of Noonan's Syndrome and has undergone several chemotherapy regimens, including A9952 Regimen A, COG MATCH with Erdafitinib, and Avastin. The best tumor response was seen while on Avastin. The patient has presented with two episodes of intratumoral hemorrhage, both after treatment with Avastin. Patient 3 presented with a sudden brain stem hemorrhage and underwent a biopsy and debulking. The pathology was consistent with a pilocytic astrocytoma with an FGFR1 mutation confirmed by Next-generation sequencing (NGS). Treatment regimens for this patient include A9952 Regimen A and Vinblastine. Patient 4 presented with acute headache and vomiting and was found to have a hemorrhagic suprasellar mass. The patient underwent tumor debulking, and pathology was consistent with low-grade glioma. NGS revealed FGFR1 and KRAS mutations. The patient received therapy as per A9952 Regimen A. Greater surveillance of this molecular and clinical finding is warranted to uncover the association between FGFR1 mutations and hemorrhage in patients with low-grade gliomas.

LGG-32. INTEGRATED BIOLOGIC, RADIOLOGIC AND CLINICAL ANALYSIS OF PEDIATRIC LOW-GRADE GLIOMAS DURING AND AFTER TARGETED THERAPY TREATMENT

Jessica W Tsai[1], Jungwhan John Choi[2,3], Hakim Ouaalam[2], Efrain Aguilar Murrillo[4], Kee Kiat Yeo[1], Jayne Vogelzang[5], Cecilia Sousa[5], Jared K Woods[5], Keith L Ligon[5], Simon K Warfield[2], Pratiti Bandopadhayay[1], Tabitha M Cooney[1]; [1]Dana-Farber/Boston Children's Cancer and Blood Disorder Center, Boston, MA, USA. [2]Department of Radiology, Boston Children's Hospital, Boston, MA, USA. [3]Department of Radiology and Medical Imaging, Cincinnati Children's Hospital, Cincinnati, OH, USA. [4]Department of Radiology, Division of Neuroradiology and Neurointervention, , Brigham and Women's Hospital, Boston, MA, USA. [5]Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA

BACKGROUND: Pediatric low grade gliomas (pLGGs) are the most common central nervous system tumor in children, characterized by driver alterations in the RAS and MAPK pathways. Genomic advances have facilitated use of molecular targeted therapies, however their long-term impact on tumor behavior remains critically unanswered. METHODS: We performed an IRB-approved, retrospective chart and imaging review of pLGGs treated with off-label targeted therapy at Dana-Farber/Boston Children's Cancer and Blood Disorders Center from 2010 to 2020. Volumetric analysis was performed for BRAFV600E and BRAF fusion/duplication driven pLGG subsets. RESULTS: Fifty-five patients were identified (dabrafenib n = 15, everolimus n = 26, trametinib n = 11, and vemurafenib n = 3). Targeted agent was used as first or second-line therapy for 58% (32/55). Median duration of targeted therapy was 0.79 years (0.01 – 4.87), and overall median follow-up was 2.50 years (0.01 – 7.39). The 1-year, 3-year, and 5-year EFS from targeted therapy initiation were 62.1%, 38.2%, and 31.8%, respectively. Mean volumetric change for BRAFV600E mutated pLGG on BRAF inhibitors was -54.11%, and median time to best volumetric response was 8.28 months (n = 12). Median time to largest volume post-treatment was 2.86 months. Mean volumetric change for BRAF fusion/duplication pLGG on MEK inhibitors was +7.34% with median time to best volumetric response of 6.71 months (n = 7). Median time to largest volume post-treatment was 2.38 months. CONCLUSIONS: Our integrated clinical and volumetric data suggest the majority of patients receiving BRAF inhibitors or trametinib achieve reduction in tumor volume while on therapy and that tumor stability can be achieved following targeted therapy cessation. Moreover, volumetric analysis shows promise as a tool to assess targeted therapeutic response in pLGGs.

LGG-33. A 40-YEAR COHORT STUDY OF EVOLVING HYPOTHALAMIC DYSFUNCTION IN 90 INFANTS AND YOUNG CHILDREN (<3Y) WITH OPTIC PATHWAY GLIOMAS

Stefania Picariello[1,2], Manuela Cerbone[3,4], Felice D'Arco[5], Hoong-Wei Gan[3,4], Patricia O'Hare[6], Kristian Aquilina[7], Enrico Opocher[6,8], Darren Hargrave[6], Helen Alexandra Spoudeas[3,4]; [1]Neuro-oncology Unit, Department of Paediatric Oncology, Santobono-Pausilipon Children's Hospital, Naples, Italy. [2]Department of Woman, Child and General and Specialized Surgery, University of Campania Luigi Vanvitelli, Naples, Italy. [3]Department of Endocrinology, Great Ormond Street Hospital for Children, London, United Kingdom. [4]Section of Molecular Basis of Rare Disease, University College London Great Ormond Street Hospital Institute of Child Health, London, United Kingdom. [5]Department of Radiology, Great Ormond Street Hospital for Children, London, United Kingdom. [6]Department of Oncology, Great Ormond Street Hospital for Children, London, United Kingdom. [7]Department of Neurosurgery, Great Ormond Street Hospital for Children, London, United Kingdom. [8]Pediatric Hematology, Oncology and Stem Cell Transplant Division, Padua University Hospital, Padua, Italy

BACKGROUND: Despite high survival, paediatric optic pathway hypothalamic gliomas are associated with significant morbidity and late mortality. Those youngest at presentation have the worst outcomes. METHODS: We aimed to assess presenting disease, tumour location and treatment factors implicated in the evolution of neuroendocrine, metabolic and neuro-behavioural morbidity in children diagnosed before their 3rd birthday and followed over four decades (1981- 2020). RESULTS: Ninety infants/young children followed-up for 9.5 years (range 0.5-25.0) were included in the study. Fifty-two (57.8%) patients experienced endo-metabolic dysfunction (EMD), the large majority (46) had hypothalamic involvement (H+) and lower endocrine event free survival (EEFS) rates. Median time to first endocrine event was 3.4 years, with EEFS declining up to 13.6 years after diagnosis. EMD was greatly increased by a diencephalic syndrome presentation (85.2% vs 46%, p=0.001), H+ (OR 6.1 95% CI 1.7 – 21.7, p 0.005), radiotherapy (OR 16.2, 95% CI 1.7 – 158.6, p=0.017) and surgery (OR 4.8 95% CI 1.3- 17.2, p=0.015), all associated with anterior pituitary disorders. Obesity occurred in 25% of cases and clustered with the endocrinopathies. Posterior pituitary disorders were recorded in 15 subjects (16.7%), only after surgery and/or as a consequence of hydrocephalus in those with suprasellar tumours and hypothalamic disease. Neurobehavioural deficits occurred in over half (52) of the cohort and were associated with H+ (OR 2.5 95% C.I. 1.1 – 5.9, p=0.043) and radiotherapy (OR 23.1 C.I. 2.9 – 182, p=0.003). CONCLUSIONS: Very young children with OPHG carry a high risk of endo-metabolic and neuro-behavioural comorbidities which deserve better understanding and timely/parallel support from diagnosis to improve outcomes. These evolve in a complex hierarchical pattern overtime whose aetiology appears predominantly determined by injury from the hypothalamic tumour location alongside adjuvant treatment strategies.

LGG-34. NEPHROLOGICAL IMPACT OF BRAF INHIBITORS IN A PEDIATRIC POPULATION OF CENTRAL NERVOUS SYSTEM TUMORS: A SINGLE INSTITUTION EXPERIENCE

Antonio Verrico[1], Marco Crocco[1], Edoardo La Porta[2], Andrea Angeletti[2], Enrico Verrina[2], Valentina Iurilli[3], Gianluca Piatelli[4], Gianluca Piccolo[1], Claudia Milanaccio[1], Maria Luisa Garrè[1]; [1]Neuro-Oncology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy. [2]Nephrology Unit, IRCCS Istituto Giannina