ences between children with NFI and controls were greater at younger than older ages. CONCLUSION: Microstructural differences were observed in WMTs in children with NFI compared to controls. These differences were not observed in other volumetric measures. The current study is the first to compare children with NFI compared to controls. These findings have implications for understanding neurocognitive deficits and gliomagenesis observed in children with NFI.

NFB-12. TRAMETINIB THERAPY FOR PEDIATRIC PATIENTS WITH REFRACTORY LOW GRADE GLIOMA OR EXTENSIVE SYMPTOMATIC PLEXIFORM NEUROFIBROMA

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OBJECTIVE: Refractory symptomatic plexiform neurofibromas (PNF) and inoperable refractory low grade gliomas (LGG) pose a clinical challenge that may be life threatening. Phase 1 and 2 clinical trials of MEK inhibition with selumetinib in inoperable PNF and LGG have demonstrated promising results. However, no data has been reported to enrollment on clinical trial. Phase 1 clinical trial for trametinib a MEK 1 and 2 inhibitor has been completed, publication is pending. Thus we have treated a series of children on a compassionate basis with extensive PN or LGG refractory disease with trametinib, as this is available in Canada. METHODS: We have treated children with trametinib on a compassionate basis in our province since 2017. Review of the clinical data regarding this therapy has been IRB approved. RESULTS: Two young patients were treated for indication of life threatening extensive PNF and have had tumor shrinkage and improvement of symptoms. Treatment has been complicated by paraneoplastic syndromes: eczema exacerbation, chondrodermatitis nodularis helica, RSF and influ enza B infection and CTCae grade 2 pneumonia. In spite of the side effects these two patients remain on treatment due to clear benefit from therapy including: improving voice quality, and respiratory compromise, hearing and dyspha gia, dysarthria and facial weakness. We will present the data of additional patients treated with trametinib. CONCLUSION: Trametinib is an effective therapy for life threatening PNF by changing the natural history of tumor growth in young children. Further data is required in terms of tolerance, efficacy and durability of response in such patients in the setting of clinical trials.

NFB-13. TRAMETINIB FOR PLEXIFORM NEUROFIBROMA AND RECURRENT LOW-GRADE GLIOMA

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BACKGROUND: Based on early clinical efficacy data, Seattle Children’s established a standard clinical practice for MEK inhibitor therapy for children with plexiform neurofibroma (PN) or recurrent low-grade glioma (LGG). METHODS: Data were collected using an IRB-approved retrospective chart review. Trametinib was prescribed off-label at 0.025 mg/kg daily for up to two years. Physical exam and laboratory monitoring were performed monthly for 3 months, then every 3 months. Retinal examination, ECHO/Eye ultrasound, and MRI were performed every 3 months for LGG; imaging for PN was dependent on tumor location. RESULTS: 30 patients received trametinib; 17 LGG, 16 PN (3 both); 22 with Neurofibromatosis, Type 1 (NF1); 16 female/13 male; median age 11 (range 4–12.6). 49% of PN patients had tumor location in the face/neck (n=10). Most common adverse events (AE) were dermatologic and gastrointestinal. Ten had dose interruption/reduction, only one discontinued therapy for AE. Six received dermatology specialty care for AE. With median follow-up of 12 months, only 3 patients had progression, one with NF1. One-year EFS was 100% for PN and 88%+7 for LGG. Driver mutations were identified in 9 of 10 tumors tested (5 BRAF fusion, 1 BRAFV600E, 1 FGFR1+NF1, 1 FGFR1+PTPN11, 1 NF1). Radiology review of response will be presented. CONCLUSIONS: This real-world pediatric cohort supports efficacy and tolerability of MEK inhibitor therapy for short-term control of plexiform neurofibroma and low-grade glioma with and without NF1. Further studies are warranted to evaluate comparative efficacy, combination therapy and duration of therapy.

NFB-14. PSYCHOSOCIAL OUTCOMES IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1 AND PLEXIFORM NEUROFIBROMAS

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OBJECTIVE: This case series seeks to examine neurocognitive outcomes, social-emotional functioning, and familial burden in young children diagnosed with Neurofibromatosis type 1 (NF1) with early growing plexiform neurofibromas (PNFs). BACKGROUND: Neurofibromatosis type 1 (NF1) is a common predisposing chronic disease arising in early childhood, with implications for understanding neurocognitive deficits and gliomagenesis observed in children with NF1. NF1 is a wide range of phenotypic variability, the primary feature of the disease is peripheral nerve sheath tumors called neurofibromas. Less is well known regarding the broader neurocognitive and social-emotional profile in patients with NF1 and PNFs, and how this impacts the quality of life of the patients and their families. This study aims to fill in these gaps in our understanding of neurocognitive and social-emotional challenges faced by children with early growing PNFs. METHODS: Participants included in this case series were children with NF1 and PNFs, aged 6-7 years old at time of evaluation. At the time of initial evaluation, participants had a confirmed NF1 diagnosis and active PNFs, according to the diagnostic criteria. All participants were evaluated using a comprehensive battery of neurocognitive assessments, including various subtests of the Wechsler intelligence scale for children, third edition (WISC-III) and the Wechsler Preschool and Primary Scale of Intelligence-Third Edition (WPPSI-III). The battery also included social-emotional assessments, including the Child Behavior Checklist (CBCL) and the Strengths and Difficulties Questionnaire (SDQ) to assess emotional challenges (e.g., executive functioning deficits, attention problems, visual-motor delays, and poor motor coordination), social-emotional challenges (e.g., symptoms of anxiety and depression, and prosocial skills), and familial distress. CONCLUSIONS: Results indicate the value of early and frequent monitoring of children with PNFs in medical systems and multi-disciplinary teams, and the importance of early intervention for both children and families.

NFB-16. MITOROPATHIES AND SUBEPENDYMAL GIANT CELL ASTROCYTOMAS: PREDICTIVE VALUE OF GERMINAL TSC1/2 MUTATIONS SCREENING IN FAMILIAL CASES

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mTOR controls several important aspects of cell function particularly in the nervous system. Its hyperactivation has been involved in tuberous sclerosis complex (TSC) and other mTORopathies as well as drug-resistant epilepsy. Mutations in TSC1 and TSC2 genes cause loss of normal inhibitory function of the mTORC1 complex, hearing and dysphagia, dia phragm paralysis and renal tumors. The goal of this ongoing study is to screen patients with tuberous sclerosis complex (TSC1/2) for mutations in TSC1 and TSC2. Patients will be screened for mTORA (mutations causing severe mental retardation and seizures) and TSC1/2 mutations. This study will be carried out using a combination of molecular techniques and multi-disciplinary teams, and the importance of family adaptability, and family cohesion is highlighted. RESULTS: A total of 50 patients were recruited for the study. TSC1 and TSC2 were screened in all patients. TSC1 and TSC2 mutations were identified in 20% of patients with TSC. The majority of these mutations were found in children with severe mental retardation and seizures. CONCLUSIONS: This study highlights the importance of genetic counseling for families with TSC. The identification of mTORA mutations in TSC1 and TSC2 highlights the importance of early intervention for these patients.