knockdown alone did not affect sensitivity to carboplatin. Our findings further support a role for ATRX loss with subsequent ALT activation in a biologic subset of NF1-associated malignancies, thereby opening an opportunity for therapeutic targeting of these aggressive tumors using specific classes of drugs.

NFB-02. TREATMENT OF PAIN AND TUMOR GROWTH IN NF2
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BACKGROUND: Neurofibromatosis Type 2 (NF2) is an autosomal dominant disorder characterized by multiple nervous system tumors. Chronic pain affects the majority of patients with NF2 and is the primary factor that contributes to decreased quality of life. There are limited therapies that effectively reduce pain in NF2, but intracranial (IV) bevacizumab has shown promise in treating NF2-related pain.

METHODS: Two patients with NF2-related pain were referred to our center for medical treatment. One patient was treated with IV bevacizumab at age 16 that improved his pain. He was critically dependent on bevacizumab for pain control and required continuous IV medication when bevacizumab was held for a surgical procedure. Following five years of bevacizumab he developed worsening toxicities including hypertension, proteinuria, and elevated hemoglobin. James transitioned to therapy with trametinib, a MEK inhibitor, and was able to wean off bevacizumab six months later. Treatment of NF2 related pain with trametinib resulted in complete resolution of his QOL symptoms, including improved medical visits, improved pain management, and decreased side effects. FUTURE IMPLICATIONS: Treatment of NF2 tumor related pain can be managed with MEK inhibitors.

NFB-03. TRAMETINIB FOR ORBITAL PLEXIFORM NEUROFIBROMAS IN YOUNG CHILDREN WITH NF1
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Neurofibromatosis type 1 (NF1), predisposes patients to benign and malignant tumors and has a lifetime risk of 10% of patients with NF1 developing a glioblastoma (GBM). Neurofibromatosis type 2 (NF2) is an autosomal dominant disorder characterized by multiple nervous system tumors. Pain from NF2 tumors can be managed with MEK inhibitors, but treatment of NF1 tumors can be challenging. We report the case of a 24-year-old man with NF1 who was treated with trametinib for orbital plexiform neurofibromas.

CASE STUDY: James is a 24-year-old who initially presented with manifestations of NF2 at age 10, and by 13 years old had developed daily pain affecting his neck, back, and lower extremity. He has multiple CNS schwannomas, meningiomas, neurofibromas, and meets clinical NF2 criteria. While genetic testing did not reveal a mutation in his gDNA, low level skipping of exon 4 via RNA splicing (likely mosaic) NF2. James’s pain was predominantly with daily physical activity, consisting of discomfort, pressure, and pressure-like sensations.

METHODS: The patient presented at age 16 to our center with concerning symptoms. The patient had a prior history of bevacizumab therapy with minimal pain improvement. A biopsy was performed and showed schwannomas. Pain control was achieved with trametinib. James has completed five cycles of temozolomide, then new left frontal GBM underwent resection with trametinib at age 22. Current trametinib therapy resulted in clinical benefit and decreased orbital pain after one week and another, with involvement of the left temporal bone found on surveillance imaging. Pathology was consistent with Langerhans cell histiocytosis (LCH) manifesting in numerous ways, from localized lesions to multisystem organ involvement secondary to a constitutively active MAPK signaling cascade often driven by BRAF mutations. While both LCH and NF1 have similar presentations on volumetric MRI, their management and response to therapy differ significantly. A novel role for trametinib may be to target LCH, and patients with NF1 may benefit from trametinib treatment.

FUTURE IMPLICATIONS: Trametinib may decrease tumor size in young children with orbital PN and may prevent progressive disfigurement.

NFB-05. AN UNUSUAL PRESENTATION OF RECURRENT LANGERHANS CELL HISTIOCYTOSIS OF THE CRANIOFACIAL REGION IN A PATIENT WITH NF2
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BACKGROUND: Neurofibromatosis Type 2 (NF2) is an autosomal dominant disorder characterized by multiple nervous system tumors. Pain from NF2 tumors can be managed with MEK inhibitors.

METHODS: We report the case of a 24-year-old man with NF2 who presented with recurrent Langerhans cell histiocytosis (LCH) of the craniofacial region. The patient was diagnosed with NF2 at age 10, and by 15 years old had developed daily pain affecting his neck, back, and lower extremity. He has multiple CNS schwannomas, meningiomas, neurofibromas, and meets clinical NF2 criteria. While genetic testing did not reveal a mutation in his gDNA, low level skipping of exon 4 via RNA splicing (likely mosaic) NF2. James’s pain was predominantly with daily physical activity, consisting of discomfort, pressure, and pressure-like sensations.

FUTURE IMPLICATIONS: Trametinib may decrease tumor size in young children with orbital PN and may prevent progressive disfigurement.

NFB-06. TREATMENT CHALLENGES IN PEDIATRIC GLOBLASTOMA MULTIFORME WITH CONCURRENT SOMATIC AND GERMLINE NF1 MUTATIONS WITH GERMLINE MISMATCH REPAIR MUTATIONS: TWO UNIQUE CASES
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INTRODUCTION: We report the first known cases of pediatric glioblastoma (GBM) with prior clinical NF1 diagnoses, one with concurrent germline Lynch syndrome (LS) and NF1, and the other with somatic NF1 mutation and germline constitutional mismatch repair deficiency (CMMRD). METHODS: Two pediatric GBM cases with prior NF1 clinical diagnoses based on neurocutaneous criteria were reviewed. Next generation sequencing and immunohistochemical staining were used for somatic and germline NF1 and MMR gene mutation detection, and for MMR protein expression, respectively. RESULTS: Sixteen year old male with prior NF1 clinical diagnosis had resection of right frontobasal GBM revealing somatic mutations of POLE and PMS2, but not NF1. His father had confirmed LS with MSH2 mutation and no neurocutaneous stigmata. Patient’s germline testing revealed POLE plus pathogenic MSH2 plus NF1 mutations. Treatment of concurrent NF1 and NF1. Treatment consisted of chemoradiation with temozolomide followed by adjuvant temozolomide with stable disease at 8 cycles. Nineteen year old male with former NF1 clinical diagnosis had 2 GBMs, first in left midbrain biopsy revealing somatic MSH2 and NF1 mutations underwent adjuvant radiation then 7 cycles of temozolomide, then new left frontal GBM underwent resection.
OPTIC PATHWAY GLIOMA (NF1-OPG): PRELIMINARY RESULTS
NEWLY DIAGNOSED, NEUROFIBROMATOSIS TYPE 1 ASSOCIATED

INTRODUCTION: Vascular endothelial growth factor receptor (VEGFR), platelet derived growth factor receptor (PDGFR), and c-KIT represent clinically and/or preclinically validated molecular targets in vestibular schwannomas. With the exception of c-KIT, studies reveal that VEGFR and PDGFR are over-expressed in schwannomas with potential therapeutic implications. Therefore, we conducted a phase II study (ClinicalTrials.gov identifier NCT01219647) to estimate the response rate to axitinib, an oral multi-receptor tyrosine kinase inhibitor targeting VEGFR, PDGFR and c-KIT, in neurofibromatosis type 2 (NF2) patients with progressive vestibular schwannomas (VS). METHODS: NF2 patients older than 18 years with at least one volumetrically measurable, progressive VS were eligible. The primary endpoint was to estimate the objective volumetric response rates to axitinib. Axitinib was given continuously in 28-day cycles for three to 36 cycles. Results were assessed every 3 months with MRI. RESULTS: Twelve eligible patients (ages: 14–66 years) were enrolled on this study. Seven of twelve patients completed 12 cycles (range: 2 to 12 cycles). We observed two imaging and three hearing responses. Best volumetric response was -53.9% after nine months on axitinib. All patients experienced drug-related toxicities, not exceeding grade 2 and hypertension, not exceeding grade 3. CONCLUSIONS: While axitinib has modest anti-tumor activity in NF2 patients, it is more toxic and appears to be less effective compared to NF1. Further study is warranted.

INTRODUCTION: Because treatment and clinical management decisions for children with NF1-OPG remain challenging, we sought to establish evidence-based guidelines. We prospectively enrolled children with newly-diagnosed NF1-OPGs, and gathered standardized clinical neuro-oncology data. METHODS: Only patients for whom the diagnosis was confirmed postmortem or recently and newly diagnosed OPGs, confirmed by central review, were eligible. Indications for obtaining the initial MRI, as well as factors associated with the decision to treat with chemotherapy or observe without treatment, were obtained. Quantitative visual acuity (VA), other ophthalmologic features, and imaging were captured at standard time points. Goal enrollment is 250 subjects. RESULTS: One-hundred thirty-three children (52% female) from 20 institutions met inclusion criteria, and were included in this preliminary analysis. Eighty-six percent of subjects were able to perform quantitative VA testing at enrollment. The most common reasons for the diagnostic MRI included screening related to NF1 diagnosis (36.8%), ophthalmologic concerns (29.1%), and non-ophthalmologic concerns (24.8%), such as head- ache. To date, twenty subjects have initiated treatment with chemotherapy, twelve (9%) at the time of the initial OPG diagnosis. Median age at OPG diagnosis was 3.1 years. Age and sex distribution were similar in subjects immediately entering the observation and treatment arms (median age 3.5 years, respectively). CONCLUSION: Most children with NF1-OPGs presented with an initial OPG diagnosis before age 2 years and were treated. Importantly, a large proportion of children are able to complete quantitative VA testing at enrollment. Once enrollment is complete, these data will help to establish evidence-based guidelines for clinical management of NF1-OPGs.

INTRODUCTION: Neurofibromatosis type 1 (NF1) is a genetic condition in which children develop learning challenges and glioma. White matter tracts (WMT) are implicated in these cognitive functions, while oligodendroglial precursors are implicated in both glommasphere and white matter development. Specific WMTrs have not been well characterized in NF1. METHODS: Twenty NF1 patients aged 1.4–17.6 years (M = 9.5 years, 24 male) and 20 age- and sex-matched controls underwent dMRI at 3T (25 directions, b = 1000 s/mm²). Automated segmentation of WMTrs extracted fractional anisotropy (FA) and mean diffusivity (MD) of 18 major WMTrs. Covariance analysis examined the effect of group (NF1/controls) on FA/MD. RESULTS: Compared to controls, children with NF1 had significantly decreased FA in 8 and increased MD in 12/18 tracts. Differences held after controlling for intracranial volume. Regression analyses for WMTrs determined the interaction of FA/MD with age for NF1 patients compared to controls. Significance was set at p < 0.05 after correcting for multiple comparisons using false discovery rate. RESULTS: Compared to controls, children with NF1 had significantly decreased FA in 8 and increased MD in 12/18 tracts. Differences held after controlling for intracranial volume. The interaction between group and age accounted for a significant proportion of the variance in FA in 9 and in MD in 16/18 tracts. FA and MD differ-