BACKGROUND: Constitutional mismatch repair deficiency syndrome (CMMRD) is a severe cancer predisposition syndrome resulting in early onset central nervous system (CNS) and other cancers. International guidelines on surveillance exist but no study systematically evaluated the efficacy of this protocol. METHODS: We surveyed all confirmed CMMRD patients in the International Replication Repair Deficiency Consortium. A surveillance protocol consisting of frequent biochemical, endoscopic and imaging (CMMRD study body MRI) studies was employed. Survival analyses and efficacy of each method were assessed. RESULTS: Surveillance data were collected from 105 CMMRD individuals from 41 countries. Of the 193 malignant tumors, CNS malignancies were the most common (44%). The surveillance protocol uncovered 49 asymptomatic tumors including 16 glioblastomas and medulloblastomas. Five-year overall survival was 89% for tumors discovered by surveillance, and 61% for symptomatic tumors (p<0.004). Similarly, 5-year survival was 82±11% and 24±6% for surveillance and non-surveillance of brain tumors (p<0.005). Yearly total body and q6 month brain MRI detected asymptomatic cancers in all but 3 symptomatic CNS gliomas. These were tumors uncovered when time between scans was >6 months as per protocol. Finally, of the low grade tumors identified asymptptomatically, 3 were low grade gliomas. All of the low grade gliomas were non-resected and survived at a median of 1.6 ± 0.9 years. CONCLUSION: These data support a survival benefit in CMMRD patients undergoing a surveillance protocol. Adherence to protocol and resection of lower grade lesions may improve survival for patients with CNS tumors.

RARE.20. MALIGNANT PERIPHERAL NERVE SHEATH TUMOR OF A CRANIAL NERVE IN AN INFANT WITH NEUROCUTANEOUS MELANOSIS
Lacey Carter, Naina Gross, Rene McNall-Knapp, and Jo Elle Peterson; University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
At one month of age, a female presented with a giant congenital nevus along lower back and thighs and neuroophelial. A ventriculoperitoneal shunt was placed. An MRI was done at six months, initially reported as normal. Five months after surgery, she presented with a large left-sided cranial nerve palsy consistent with a malignancy. The MRI revealed a 3.8 x 3.7 x 3.4 cm right cerebellopontine angle mass extending into Meckel’s cave and foramen ovale along with leptomeningeal disease extending from the mass along the entire length of the spinal cord. Retrospective review of prior MRI revealed subtle leptomeningeal enhancement concerning for neurocutaneous melanosis (NCM). Given the leptomeningeal disease, family elected for open biopsy and debulking of lesion instead of aggressive resection. Histologically, the lesion showed hypercellularity with a significant number of melanocytes. Immunohistochemical stains for 15 melanomas (NCM) were negative, excluding melanoma. A negative myogenin stain ruled out malignant peripheral nerve sheath tumor (MPNST). Given the course of the disease, a surveillance protocol was initiated and the patient was discharged with hospice. She died 25 days after surgery. Cranial nerve MPNST is rare. MPNST in patients with NCM has not previously been reported to our knowledge.
in 21 patients including 13 in MB survivors. Mutations were inherited in 58/66 (88%) of cases in which inheritance could be tested and de novo in 8. In 6/67 families (9%), >2 children were diagnosed with a MB. CONCLUSION: In this cohort, de novo and inherited SUFU mutations carried by MB patients are the most frequent tumor suppressor mutations. In MB, in infants is the most frequent tumor but the spectrum also includes typical Gorlin syndrome tumors (BCC, meningiomas, and ovarian stromal/lubricous tumors) either as first tumors or as second malignancies. This broad tumor spectrum and the high risk of second malignancies justify the implementa-
tion of specific cancer surveillance programs.

RARE-22. GERMINE PATHOGENIC VARIANT C.1552G>A;p.E518K IN DGCR8 CONFRS SUSCEPTIBILITY FOR SCHWANNOMATOSIS AND THYROID TUMORS
Anne-Sophie Chong1, Javad Nadaf2, Elia Grau9, Maria Apellanz-Ruiz1,2, Somayeh Fakhimi2, Ari Sasaki1,4, HyEum Han1,2, Robert Turcotte1,4, Karl Mischack1,4, Christian Thomae1,4, Ruben Wagenknecht2,3, Angela Bassendine1, Ougur Mete3,9, Marc Pusztaszeri2, Werner Paulus1, Robert Berghues1, Reiner Siebert1,2, Steffen Albrecht3, Martin Hasselblatt4, Conxi Lazaro1,2, Alexander Teule1, Marc Fabian4, Joan Brunet1, Robert Hibiya1, Rabea Okada1, Fabian3, Hiroaki4, Robert3, Martin5, Memorial Sloan Kettering Cancer Center, New York, NY, USA, 6Weill Medical College of Cornell University, New York, NY, USA

Neurocutaneous melanocytosis (NCM) is a rare disease characterized by excessive proliferation and deposition of melanocytes in the leptomeninges and brain parenchyma, occurring in children with large congenital melanocytic nevi (LCMNs). Manifestations of NCM range from asymptomatic CNS melanocytic depositions to cranial neuropathies, choristomas, and hydrocephalus. Patients with NCM are at risk for malignant melanoma. We conducted a retrospective, single-institution study of patients with LCMN evaluated at Memorial Sloan Kettering Cancer Center from June 2000 to January 2020. Of 55 patients studied, 15 had no radiographic NCM, and 40 had radiographic NCM at initial evaluation. MRI findings included: focal melanocytosis (33), diffuse leptomeningeal disease (4), solid melanoma (3). Malformations were identified in 13, including arachnoid cyst (4), congenital hydrocephalus (4), Dandy-Walker malformation (3), and tetradic cord (1). Twenty-one patients completed imaging once and were followed clinically. Seventeen with serial imaging (10 with focal melanocytosis, 7 with normal MRI) remained stable over a median 24-month follow up range (up to 12+). For this large cohort of germline progression of NCM without melanoma. Malignant melanoma developed in 11 patients, 5 with focal melanocytosis on initial imaging. Median time from focal melanocytosis identification to melanoma diagnosis was 80 months (range: 18–200). Median age at melanoma diagnosis was 11.25 years. Somatic mutations were observed in 5 with CDKN2A (1), 1 with CDK4 (1), 1 with CDKN1B (1), and 1 with CDKN1C (1). The median survival from melanoma diagnosis was 9.1 months (range: 1–60+). Focal NCM on neuroaxis imaging does not predict time to transformation to malignant melanoma. Serial imaging is not indicated in absence of disease-modifying treatment. Clinical follow up of at-risk individuals is essential in early identification of complications.

RARE-25. RETINAL ASTROCYTOMA MTOR INHIBITOR THERAPY IN TUBEROUS SCLEROSIS MOSAICISM
Naomi Evans1, Katherine Patton2, Harinder Kaur Gill3, and Juliette Hukin1
1Children’s and Women’s Health Centre of British Columbia, Vancouver, BC, Canada, 2Vancouver General Hospital, Vancouver, BC, Canada, 3University of British Columbia, Vancouver, BC, Canada

INTRODUCTION: Everolimus is an inhibitor of mTORC1 (mammalian target of rapamycin complex 1), it is Health Canada and FDA approved for neurofibromatosis type 1 (NFI) and tuberous sclerosis complex (TSC). There is little data available in regards to this treatment of TSC associated retinal astrocytoma (RA). Although the behaviour of RA is often indolent or slowly progressive, aggressive behaviour with retinal detachment and neovascularisation has been reported in several patients. Definite TSC diagnosis is established when either two major features or one major and two minor features are present. Probable TSC diagnosis is established when one major plus one minor feature is present. METHODS: We report a child with probable TSC mosaicism with negative serum NGS for TSC but RA and retinal achromic patch on the left. A left retinal peripapillary astrocytoma around optic nerve and very close to fovea was noted. There was concern that if it grew or there were to be any leakage it would cause visual impairment. This lead to therapy with everolimus 4.5 mg/m2 aiming for level between 5 and 10 mcg/L. RESULTS: This boy has had a gradual reduction of the RA over the last 20 months, with healthy retina in the region no longer occupied by the lesion and preserved vision. He has tolerated therapy well with occasional mouth ulcers. CONCLUSION: mTORC1 inhibition is effective therapy to preserve vision in the setting of retinal astrocytoma and tuberous sclerosis mosaicism.

RARE-24. LARGE CONGENITAL MELANOCYTIC NEVI AND NEUROCUTANEOUS MELANOCYTOSIS: A RETROSPECTIVE CASE SERIES
Lugenia Elie, Elise Emrin, Stephanie Suer1, Ashfaq Marghoobi1, Sofia Haque1, and Yasmin Khakoo2,3,4
1Memorial Sloan Kettering Cancer Center, New York, NY, USA, 2Weill Medical College of Cornell University, New York, NY, USA

Neurocutaneous melanocytosis (NCM) is a rare disease characterized by excessive proliferation and deposition of melanocytes in the leptomeninges and brain parenchyma, occurring in children with large congenital melanocytic nevi (LCMNs). Manifestations of NCM range from asymptomatic CNS melanocytic depositions to cranial neuropathies, choristomas, and hydrocephalus. Patients with NCM are at risk for malignant melanoma. We conducted a retrospective, single-institution study of patients with LCMN evaluated at Memorial Sloan Kettering Cancer Center from June 2000 to January 2020. Of 55 patients studied, 15 had no radiographic NCM, and 40 had radiographic NCM at initial evaluation. MRI findings included: focal melanocytosis (33), diffuse leptomeningeal disease (4), solid melanoma (3). Malformations were identified in 13, including arachnoid cyst (4), congenital hydrocephalus (4), Dandy-Walker malformation (3), and tetradic cord (1). Twenty-one patients completed imaging once and were followed clinically. Seventeen with serial imaging (10 with focal melanocytosis, 7 with normal MRI) remained stable over a median 24-month follow up range (up to 12+). For this large cohort of germline progression of NCM without melanoma. Malignant melanoma developed in 11 patients, 5 with focal melanocytosis on initial imaging. Median time from focal melanocytosis identification to melanoma diagnosis was 80 months (range: 18–200). Median age at melanoma diagnosis was 11.25 years. Somatic mutations were observed in 5 with CDKN2A (1), 1 with CDK4 (1), 1 with CDKN1B (1), and 1 with CDKN1C (1). The median survival from melanoma diagnosis was 9.1 months (range: 1–60+). Focal NCM on neuroaxis imaging does not predict time to transformation to malignant melanoma. Serial imaging is not indicated in absence of disease-modifying treatment. Clinical follow up of at-risk individuals is essential in early identification of complications.

CONCLUSION: In this large cohort of germline progression of NCM without melanoma. Malignant melanoma developed in 11 patients, 5 with focal melanocytosis on initial imaging. Median time from focal melanocytosis identification to melanoma diagnosis was 80 months (range: 18–200). Median age at melanoma diagnosis was 11.25 years. Somatic mutations were observed in 5 with CDKN2A (1), 1 with CDK4 (1), 1 with CDKN1B (1), and 1 with CDKN1C (1). The median survival from melanoma diagnosis was 9.1 months (range: 1–60+). Focal NCM on neuroaxis imaging does not predict time to transformation to malignant melanoma. Serial imaging is not indicated in absence of disease-modifying treatment. Clinical follow up of at-risk individuals is essential in early identification of complications.

RARE-23. NOVEL NFI MUTATIONS IN TWO OCCURRENCES OF GLOBLASTOMA MULTIFORM IN A PATIENT WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY SYNDROME Kaylin Ute4, Jens Reuter4, Lei Li4, Devon Evans4, Jeffrey Florman5, and Stanley Chalifet4, Meine Medical Center, Portland, ME, USA, 2Jackson Laboratory, Bar Harbor, ME, USA

Constitutional mismatch repair deficiency (CMMRD) syndrome is a rare cancer predisposition syndrome in children. Its main associated tumor types include brain and CNS tumors, hematologic malignancies, intestinal polyps and colorectal tumors, and other malignancies. Tumor genesis within this population is highly complex and poorly understood. We describe a case of a patient with two occurrences of glioblastoma multiforme (GBM), each with unique NFI mutations. The patient is a female with CMMRD who was first diagnosed with GBM of the right frontal lobe in 2013. She subsequently underwent gross total resection, radiation to the field and concomitant and maintenance therapy with Temozolomide and Everolimus, due to high suspicion for NF-1. Genetic studies didn’t show NF-1, instead revealing a diagnosis of CMMRD. Molecular testing of the GBM showed a high mutational burden and an NF1 mutation. Later, screening revealed stage IV colon cancer, for which she underwent subtotal colectomy, partial liver resection and chemotherapy. Molecular testing from the colon cancer found a hypermutator malignancy without mutations in NFI. Surveillance imaging detected a mass at the original site of her GBM, for which she had a resection. Notably, the genetic profile of the second tumor substantially different from the original tumor and the colon cancer sample, but had new mutations in NF-1. These findings highlight the significant variability in the genetic profiles of tumors in the context of CMMRD. It is also worth consid-