BRAF-V600E mutations may benefit from upfront targeted therapy. Prospective clinical trials comparing the efficacy of BRAF inhibitors versus standard chemotherapy in LGG with BRAF mutations are urgently needed.

### LGG-24. CARBOPLATIN-INDUCED HEMATURIA IN A PEDIATRIC PATIENT WITH LOW-GRADE GLIOMA AND REVIEW OF LITERATURE

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OBJECTIVE: In this case report, we present a pediatric patient with gross hematuria and hydroureteronephrosis associated with high dose carboplatin. Given the paucity of literature on the subject, we also conduct and present a review of cases. CASE PRESENTATION: A 6-year-old Caucasian female with history of Type 1 neurofibromatosis was undergoing treatment for a low-grade glioma with monthly high dose carboplatin (560 mg/m$^2$). After 8$^{th}$ dose out of 13, the patient developed severe nausea and vomiting and was admitted for dehydration. She was noted to have microscopic hematuria. After 9$^{th}$ dose, the patient again developed severe nausea, vomiting and gross hematuria with clots. She was admitted and treated with IV hydration. Renal ultrasound showed newly developed bilateral hydroureteronephrosis. Coagulation studies were normal. Multiple cultures and viral studies were negative. Hematuria cleared spontaneously after 4 days of aggressive hydration. RESULTS: Subsequent carboplatin was given with aggressive hydration and minimized nausea/vomiting and no hematuria was observed. Literature review revealed only 4 reported cases of carboplatin-induced hematuria, including only one pediatric case that occurred in a patient with concurrent thrombocytopenia. Carboplatin may exhibit toxicity to the transitional epithelial cells of the urogenital tract causing hemorrhage from the renal pelvis and ureters. If untreated, this may lead to urinary outflow obstruction and subsequent obstructive nephropathy. CONCLUSION: We present a rare toxicity, gross hematuria caused by high-dose carboplatin treatment. Providers should be aware of this rare toxicity and provide timely hydration and supportive care to prevent development of obstructive kidney injury and/or renal failure.

### LGG-25. A PHASE 2 STUDY OF TRAMETINIB FOR PATIENTS WITH PEDIATRIC GLIOMA WITH ACTIVATION OF THE MAPK/ERK PATHWAY. TRAM-01

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BACKGROUND: Pediatric low-grade gliomas (PLGG) are the most frequent brain tumors in children. It is now known that the majority of PLGG have activation of the MAPK/ERK pathway. We hypothesize that we will observe responses in recurrent/refractory PLGG treated with trametinib. METHODS: This is a multicenter phase II including three progressing/refractory PLGG groups: NF1 patients, KIAA1549-BRAF fusion patients and patients with other activation of the MAPK/ERK pathway (excluding V600E). Patients will receive daily oral trametinib for a total of 18 cycles of 28 days. A total of 104 patients will be enrolled in seven Canadian centers. Secondary objectives include the assessment of progression-free survival, tolerability of trametinib, serum levels of trametinib and evaluation of quality of life during treatment. RESULTS: As of January 7 2020, 28 patients have been enrolled (NF1: 6 patients, KIAA1549-BRAF fusion: 17, other: 5 including 3 patients FGFR1 alteration). Median age is 8.5 years (range 2.5–25.4 years). Median follow-up is currently 4.6 months (range 0.16–14.7 months). Twenty patients are currently evaluable. Best response includes: 1 complete response (5%), 3 partial response (15%), 4 minor response (20%), 8 stable disease (40%), 4 progressive disease (20%). 8 patients (28,5%) discontinued treatment: 4 for progressive disease, 3 adverse event (alanine aminotransferase increase), 1 withdrew. CONCLUSION: Trametinib is potential effective targeted therapy for patients with recurrent/refractory PLGG. Overall treatment is well tolerated. This ongoing trial will continue to gather data on response rate, duration of response and safety of trametinib for PLGG.

### LGG-26. DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR (DLGNT) IN CHILDREN: DIFFERENT CLINICAL PRESENTATIONS AND OUTCOMES

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Diffuse leptomeningeal glioneuronal tumor (DLGNT) is an extremely rare disease, newly recognized in the 2016 WHO classification of tumors of the CNS. Most DLGNTs are low-grade neuroepithelial tumors with variable elements of neuronal/neurocytic and glial differentiation, have diffuse leptomeningeal enhancement on MRI, and typically harbor *KIAA1549-BRAF* fusions. Other alterations, such as the *BRAF* V600E substitution, are less common. Here, we present three cases of DLGNT with different presentations and outcomes. The first patient is a 2yr-old male with KIAA1549-BRAF fusion, and was treated with Carbo/VCR chemotherapy after a biopsy, with resultant ongoing stable disease for 3.5 years. The second patient, an 8yr-old male had the *BRAF* V600E point mutation and was treated with conventional chemotherapy (VCR/carboplatin). On progression, he received the BRAF inhibitor vemurafenib, achieving a complete response which last 14 month. The third patient, a 27 month old male, harbored a KIAA1549-BRAF fusion and was treated at diagnosis with the MEK inhibitor trametinib. The tumor has been radiographically stable in the context of clinical improvement for 21 months since the treatment initiation, ongoing 24 month. In summary, we present further evidence of MAPK pathway alterations in children with DLGNT. We describe a range of molecular presentations and clinical outcomes, including one patient treated with conventional chemotherapy with further stabilization of disease during 3.5 years and two patients who were successfully treated with targeted therapy.

### LGG-27. TARGETED THERAPY FOR PEDIATRIC LOW-GRADE GLIOMAS AND PLEXIFORM NEUROFIBROMAS WITH TRAMETINIB

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BACKGROUND: Targeted therapy aimed at modulating the RAS/RAF/MEK/ERK pathway is of increasing interest for patients with plexiform neurofibromas and low-grade gliomas. Trametinib is an FDA-approved MEK inhibitor that has little published pediatric experience to date. METHODS: A retrospective chart review of patients treated with trametinib for low-grade gliomas (LGG) and/or plexiform neurofibromas (PN) between 2015–2018 was conducted at Children's Hospital Colorado. Data collected included patient demographics, lesion location, Neurofibromatosis type 1 (NF1) status, best response of PN/LGG to trametinib, duration of trametinib therapy, and reported toxicities at least possibly attributed to trametinib. RESULTS: Thirty (57% male; 73% NF1) patients were identified. Sixteen (53%) patients had PN only, 12 (40%) had LGG only, and two (7%) patients had both PN and LGG. The most common LGG location was the optic pathway/hypothalamus (72%). The most common location of PN was the face (63%). Two-thirds (8/12) of patients with LGG had a BRAF alteration or NF1 mutation. The median age at start of trametinib therapy was 9.9 years (range, 2.0 – 18.8 years). The median duration of trametinib therapy was 0.8 years (range 0.1 – 2.9 years). The most commonly reported adverse event was rash. No patients developed retinal toxicity or cardiotoxicity. Only two (7%) patients discontinued for toxicity and one (3%) for progressive disease. CONCLUSIONS: Trametinib can be administered without significant toxicity to children with PN or LGG. Clinical benefit is noted in this cohort; however, prospective clinical trials are necessary to characterize efficacy formally.