diagnostics, the Pediatric Targeted Therapy (PTT) 2.0 program aims at the improvement of diagnostic accuracy and detection of actionable alterations for pediatric high-risk patients. The impact of these analyses on clinical management varied. Methods: Pediatric patients with relapsed progressive tumors after standard of care treatment were included, independent of histological diagnosis. Formalin fixed paraffin embedded material and a blood sample for germline correction were requested. DNA methylation array, targeted gene panel sequencing (130 genes), RNA and Sanger sequencing in selected cases, and immunohistochemistry (IHC) of selected markers (pERK, pAKT, pS6, PD-1) were performed. A questionnaire-based follow-up was used to determine the clinical impact of the analysis. Results: We enrolled n=263 patients from February 2017 to February 2019. Complete molecular analysis was possible for n=260 cases (99%). The most common entities were brain tumors (n=172/260, 65%). In brain tumors, DNA methylation array alone allowed robust diagnostic classification (score of >0.9) in n=104/172 cases (60%). Actionable targets as detected by copy number calculation, gene panel sequencing, RNA sequencing and IHC were found in n=94/172 (55%) brain tumor cases. The most common actionable targets in brain tumors were MAPK (pERK, BRAF fusions, BRAF V600E), mTOR (pS6), PI3K (pAKT), CDKN2A (pAKT)/CDKN2A/B loss, and immune check- points (PD-1). Pathogenic germline alterations with clinical relevance were identified in n=12/172 brain tumor cases (6.9%) and were confirmed by Sanger sequencing, s/n 12 (41%) of which were previously unknown. Clinical follow-up of subsequent treatment and outcome are ongoing. Conclusion: The combination of next-generation sequencing technologies such as targeted sequencing arrays and targeted sequencing in addition to selected IHC markers added robust information with regard to diagnosis and actionable alterations. The impact on clinical decision-making and on outcome is currently being evalu- ated.

EPTC-07. ID1 IS A KEY TRANSCRIPTIONAL REGULATOR OF DIPG TUMOUR INVASION AND IS TARGETABLE WITH CANNABIDIOL Viveka Nand Yadav1, Micah K. Harris1, Chase Thomas1, Steffanie Tallarid1, Rinette Woo2, Robert Siddaway1, Jingming Qin1, Jessica R. Cummings1, Brendan Mullan1, Ruby Sara1, Raghavendra1, Michael Maclellan1, Xinhong Cao1, Maria G. Castro1, Pedro R. Lowenstein1, Rajen Mody1, Arul Chinnavay1, Cynthia Hawkins1, Pierre Desprez1, Sean McAllister1, Srimat Venet1, and Carl Koschmann1. 1University of Michigan, Ann Arbor, MI, USA, 2California Pacific Medical Center Research Institute, San Francisco, CA, USA, 3University of Toronto, Toronto, Canada

Diffuse intrinsic pontine gliomas (DIPGs) are lethal pediatric brain tumors with no effective therapies beyond radiation. The highly invasive nature of DIPG is key to its aggressive phenotype, but the factors and mechanisms contributing to this aggressive invasion are unknown. Inhibitor of DNA binding (ID1) proteins, key regulators of lineage commitment during embryogenesis, are implicated in tumorigenesis in multiple human solid tumors. Prior work identified recurrent H3F3A mutations in DIPG. Knockdown of primary human H3.3K27M-DIPG cells with CBD could potentially be an effective therapy for DIPG.

EPTC-08. TRIAL WORKING GROUPS FOR PAEDIATRIC BRAIN TUMOURS Ruman Rahman1, David Walker1, Emma Campbell1, and Kristina Aquilina2. 1The University of Nottingham, Nottingham, UK, 2Great Ormond Street Hospital, London, UK

Introduction: Brain tumours are the biggest cancer killer in children and young adults. Several major developments have the potential to change the treatment of brain tumours in children. These include ultrasound-mediated blood-brain barrier disruption, convection enhanced delivery, polymer delivery systems and electric field therapy, as well as intra-arterial, intra-CSF and intra-nasal chemotherapy. To date, there have been very few clinical trials to evaluate any of these. The science and technology underlying these developments is not traditionally embedded within the standard paediatric neuro-oncology network. In addition, custom-built hardware, novel sur- gical approaches and, in some cases, the testing and humanisation of implantable devices, add difficulty at the regulatory level. Methods: The authors par- ticipated in an international workshop funded by the charity Children with Cancer UK in 2016, where different experimental techniques aimed at optimising CNS drug delivery were discussed. Following this workshop and two subsequent workshops run by the CBTDDC (Children’s Brain Tumour Drug Delivery Consortium) in 2018 and 2020, the CBTDDC and the recently developed ITCC (Innovative Therapies for Children with Cancer) brain tumour group started working together to set up a new initiative. This group aims to develop CNS-delivery focused trial working groups for paediatric brain tumours. Results: We have assembled a prestigious steering group, comprising international researchers and clinicians with expertise in diverse aspects of translational and clinical research in CNS drug delivery. At our first group meeting in March, participants will discuss the most effective ways of translating the emerging drug delivery modalities into clinical trials. Prioritised actions will be taken forward and the group will reconvene to discuss developments and next steps at a workshop in the Autumn. Conclusion: We present this abstract to the SNO Paediatric conference to raise awareness of this initiative with the large number of relevant stakeholders who will be attending the event.

EPTC-09. CNS LEVELS OF PANOBINOSTAT IN A NON-HUMAN PRIMATE MODEL: COMPARISON OF BLOOD AND CEREBROSPINAL FLUID PHARMACOKINETIC METHODS AND MALDI NNABDIOLID Katherine Warren1, Cynthia Lester McCully2, Rafael Cruz Garcia2, Sylvia Stopyk1, Michael Regan1, Thet Aye2, Sara Zimmerman3, Cody Peer4, Josh Kramer4, Matthew Breed5, W. Douglas Figg6, and Nathalie Agar2. 1DPCI, Boston, MA, USA, 2NCI, Bethesda, MD, USA, 3Bigham and Women’s Hospital, Boston, MA, USA, 4NIH, Bethesda, MD, USA

 Adequate exposure (effective concentration over time) of a therapeutic agent at its site of action is essential for tumour efficacy. The highly invasive nature of DIPG is key to its aggressive phenotype, but the factors and mechanisms contributing to this aggressive invasion are unknown. Inhibitor of DNA binding (ID1) proteins, key regulators of lineage commitment during embryogenesis, are implicated in tumorigenesis in multiple human solid tumors. Prior work identified recurrent H3F3A mutations in DIPG. Knockdown of primary human H3.3K27M-DIPG cells with CBD could potentially be an effective therapy for DIPG.
inary clinical activity in an adult phase 1 study. Methods: Five children with progressive/refractory CNS tumors harboring an FGFR gene alteration following prior therapy were treated with DebiO1347 at Memorial Sloan Kettering Cancer Center on single patient cohorts using the 20 mg tablet formulation at the adult recommended phase 2 dose (80 mg/1.73 m2 on 5 days). Toxici6ties were graded using CTCAE v5.0 and imaging response assessments were performed every 8-12 weeks. RE65 for 22q11 deletion was identified after prior unsuccessful treatment-refractory leptomeningeal sur6ery was hyperphosphataemia, ALT increased and hypoalbuminemia (4% events). Two patients met criteria for partial response and two patients had stable disease. A 13 month-old patient with a spinal cord high-grade glioma harboring two FGFR3 mutations (V592M, K577E) had tumor re6uction of 91.7% maintained for 12 months. A 26-month-old patient with a pilomyxoid astrocytoma harboring an FGFR1-TACC fusion had a tumor reduction of 74.5% maintained for 9 months. Molecular characterization of recurrent tumor from this patient demonstrated an NFI deletion as a novel mechanism of acquired resistance to FGFR inhibition. Prolonged disease stabilization was noted in an eight year-old patient with metastatic suprasellar pilomyxoid astrocytoma harboring an FGFR1 mutation (9 months) and in a 14-year-old patient with posterior fossa glio-neuronal tumor harboring an FGFR3-TACC fusion (24 months and ongoing.). Con6usions: DebiO1347 demonstrated tolerable toxicity and promising anti-tumor efficacy in pediatric patients with refractory FGFR altered gliomas. Specific attention to growth velocity and clinical symptoms with incorporation of imaging assessment of bone growth is warranted. Candidate markers (FGFR1 V592M and K577E SNVs, FGFR-TACC fusions) may guide patient selection. Further studies in this population are warranted.

EPTC-11. RURALITY INDEX SCORE AND PEDIATRIC NEURO-Oncological OUTCOME IN ONTARIO Michelle Kameda-Smith1, Gregory Pond, Forough Farrokhyar, and Hsien Siew; McMaster University, Hamilton, ON, Canada

Introduction: Rapid access to neurosurgical decisions and definitive management are vital for the outcome of neuroc6rital patients. There are inherent challenges of providing services to rural communities. This study aimed at identifying rurality as a significant factor towards reduced follow-up compliance in the higher RIO score cohort with length of follow up, indicating rurality was not a significant factor (Continuous p-0.05). The median distance to the nearest pediatric neurosurgical hospital was 59.6 km. The rurality index score (RIO) was 0 in 38.8% of children with the majority of patients with a RIO score of <39. The ON-MARG identified 31.9% of patients living in communities with low concentration of individuals without income from employment. A higher RIO score was not a significant factor (Continuous p=0.02, trend p=0.20) associated with length (G3) of follow up, indicating rurality was not a significant factor for determining compliance to (G4) clinical follow-up. However, a trend towards reduced follow-up compliance in the higher RIO score cohort was identified: rurality and social determinants of health of the region pediatric neuro-oncological patients reside were not associated with patient outcome but a trend towards lower follow-up compliance was identified when children were from regions with RIO>39. Implementation of telehealth follow-up for these patients may overcome barrier to clinical follow-up.[G5]

EPTC-12. NATIONAL MULTICENTERED RETROSPECTIVE REVIEW OF DEMOGRAPHIC, TUMOUR AND INTRAOPERATIVE FEATURES ASSOCIATED WITH THE DEVELOPMENT OF CEREBELLAR MUTISM AFTER PEDIATRIC POSTERIOR FOSSA TUMOUR RESECTION Michelle Kameda-Smith1, Cameron Elliot2, Hanna Moore2, Nicholas Sader1, Michael Tso1, Mosaab Alsuwaihel3, Ayoub Farrokhyar2, Olivia Ajani1, Blake Yarascavitch4, Adam Fleming5, Vivek Mehra6, Forough Farrokhyar2, Ali Yikilmaz2, Nina Stein3, and Sheila Singh1

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Background: Cerebellar mutism (CM) is a condition characterized by a significant lack or loss of speech in children following posterior fossa (PF) surgery. The biological origin of CM remains largely unclear and remains the subject of ongoing debate. Despite multidisciplinary rehabilitative interventions, the outcome is less favorable than initially described.

EPTC-13. SINGLE INSTITUTION RETROSPECTIVE ANALYSIS OF TUMOR MUTATIONAL BURDEN AND SURVIVAL IN PEDIATRIC BRAIN TUMORS Rose Paris1, Roshal Patel1, and Lauren Wenstrup2; Albany Medical College, Albany, NY, USA, 1Albany Medical Center, Albany, NY, USA

Tumor mutational burden (TMB) has been studied across numerous cancer types as a means of risk stratification. To examine the prognostic relevance of TMB to pediatric central nervous system (CNS) tumors, we conducted a retrospective analysis of patients at Albany Medical Center diagnosed from 2012 to 2019. Patients were <21 at diagnosis, had a primary CNS tumor and available genomic data. Forty-seven patients were included – 22 low-grade gliomas, 10 high-grade gliomas, 5 medulloblastomas, 4 ependymomas, 2 choroid plexus carcinomas, and 5 other CNS tumors. The majority of final tumor histology was available in 90.3% of cases. The median age at diagnosis was 10 years (1–19), and 47% female. Median TMB was 1 mutation per megabase (mut/mb) range 0–6. Nine patients did not have available TMB data. Twenty-seven patients had driver mutations and other alterations implicated in cancer development including, including BRAF-V600E mutation (n=2), NF1 loss (n=5), FGFR1 amplification (n=4), TP53 inactivation (n=4), BRAF V600E mutation (n=3), and H3F3A K28M mutation (n=3). Patients with low TMB (<3 muts/mmb or 24) versus high TMB (>3 muts/mmb or 14) had a survival of 77% versus 71%, respectively, at last follow-up. Of note, all but one patient in the low TMB cohort had localized disease at diagnosis versus three in the high TMB cohort. High TMB was more prevalent in high-grade (45%, 9/20) versus low-grade histologies (22%, 4/18). Patients with BRAF alterations had low TMB (<3 muts/mmb) with all patients surviving last follow up. Of the eight deaths observed (median 18 months from diagnosis) TMB was high in 4, low in 3, and unknown in 1; all had high-grade histology. Although limited, our data suggests higher TMB may be associated with worse survival. This analysis will be expanded via a multi-institutional review of TMB and genomic alterations in pediatric CNS patients to better identify high-risk patients requiring alternative treatment strategies.

EPTC-14. GD2 CAR T-CELLS MEDIATE CLINICAL ACTIVITY AND MANAGEABLE TOXICITY IN CHILDREN AND YOUNG ADULTS WITH H3K27M-MUTATED DIPG AND SPINAL CORD DMG Robhie Mazer, Sneha Ramakrishna, Aaron Mochizuki, Shubnum Patel, Harsha Chinnaswamy, Kristen Yeon, Liara Schultz, Rebecca Richards, Cynthia Campan, Agnes Reschke, Jaisa Mahdi, Angus Martin Shaw Toland, Christina Baggott, Sharon Mavroukakis, Emily Egetele, Jennifer Moon, Kayla Land, Lindsay Brown, Adam Zandieh, John Tamaresis, Anne Marcy, Michael Kunicki, Michelle Fujimoto, Zach Ehlinger, Sreerodya Kurra, Timothy Cornel, Sonni Partap, Paul Fisher, Gerald Grant, Hannes Vogel, Bita Salar, Kara Davis, Steven Feldman, Crystal Mackall, and Michelle Monje; Stanford University School of Medicine, Stanford, CA, USA

Background: We previously discovered high expression of the carbohydrate GD2 on H3K27M+ gliomas and demonstrated preclinical efficacy of intravenous (IV) GD2-targeted chimeric antigen receptor (CAR) T-cells in preclinical models of H3K27M-mutated diffuse intrinsic pontine glioma (DIPG) and diffuse midline gliomas (DMGs). We are now conducting a Phase 1 clinical trial (NCT04196413) of autologous GD2-targeting CAR T-cells for H3K27M+ DIPG and spinal cord DMG. Here we present the

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