Given the treatment refractory nature of CM, central to its management is prevention. Methods: A national multi-centered retrospective review of all the children undergoing posterior fossa resection at 4 Canadian academic centers was undertaken. Patient demographics, surgery-related features suggested to be associated with the post-operative development of CM were reviewed to identify pre-operative and intra-operative factors that may predict post-operative CM occurrence. Results: 258 pediatric patients with histologically confirmed primary posterior fossa tumors received resection surgery. The overall incidence of CM was 6.74 years (SD 4.60) and 42.2% were female. Frozen section was available in 90.3% of cases. The majority of final tumour histology was medulloblastoma (35.7%), pilocytic astrocytoma (32.6%), and ependymoma (17.1%) and exophytic glioma (12.2%). Intra-operative impression of adherence to the floor of the 4th ventricle was negative in 47.7%, positive in 36.8% of cases. The extent of resection assessed intraoperatively as gross total resection was 69.8% of cases. Intra-operative abrupt changes in blood pressure and/or heart rate was identified in 19.4% and 17.8% of cases. CM was experienced in 19.5% of patients (N=30), with the majority of cases identified by post-operative day 7. The clinical resolution of CM as mainly assessed by a neurosurgeon (86%) and was complete, significantly resolved, slight improvement, no improvement or deterioration in 56.0%, 8.0%, 20.0%, 14.0%, 2.0% respectively. Conclusion: As a devastating surgical complication, identifying and understanding the biological origin of CM is the first step to complication avoidance. Maximal safe resection irrespective of intra-operative pathology remains the goal to avoid the devastating complication of CM.

EPTC-13. SINGLE INSTITUTION RETROSPECTIVE ANALYSIS OF TUMOR MUTATIONAL BURDEN AND SURVIVAL IN PEDIATRIC BRAIN TUMORS

Rose Parisi1, Roshal Patel1, and Lauren Weintraub2; 1Albany Medical College, Albany, NY, USA, 2Albany 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 review of patients as an effort to maintain critical care structure for rural citizens. The relationship between rurality, marginalization and health outcomes has been identified as associated with higher mortality rates and higher rates of many diseases[1]. Methods: Employing linked administrative databases, we retrospectively analyzed a population-based cohort of patients diagnosed with a pediatric brain tumor between 1996 to 2017 in Ontario, Canada. The Ontario Marginalization Index was employed as a surrogate for rurality providing an overall Rurality Index for Ontario (RIO) in addition to the 2016 Ontario Marginalization Index (ON-MARG). Results: Of 1457 patients included, 54.0% were male, 277 of whom were diagnosed in infancy (i.e., < 3 years of age). Income quintile was evenly distributed with 11.5% classified as living in a rural area of Ontario. The median[2] 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=0.092, median 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: Rulality 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-14. GD2 CAR T-CELLS MEDIATE CLINICAL ACTIVITY AND MANAGEABLE TOXICITY IN CHILDREN AND YOUNG ADULTS WITH H3K27M-MUTATED DIPG AND SPINAL CORD DMG

Rubhie Maizner, Sneh RamaRajkumar, Aaron Mohrazkis, Shabnum Patel, Harshini Chinnasamy, Kristen Yeom, Liara Schultz, Rebecca Richards, Cynthia Campen, Agnes Reschke, Jaisa Mahdi, Angus Martin Shaw Toland, Christina Baggott, Sharon Mavroukakis, Emily Eglez, Jennifer Moon, Kayla Land, Lindsay Rassam, Shreya Khanna, John Tamassas, Anne Marcy, Michael Kunicki, Michelle Fujimoto, Zach Ehlinger, Sreevidya Kurra, Timothy Cornel, Sophia Partap, Paul Fisher, Gerald Grant, Hannes Vogel, Bita Sahat, Kara Davis, Steven Feldman, Crystal Mackall, and Michelle Monge; Stanford University School of Medicine, Stanford, CA, USA

Background: We previously discovered high expression of the dopamine-glycosyl 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 I clinical trial (NCT04194641) of autologous GD2-targeting CAR T-cells for H3K27M+ DIPG and spinal cord DMG. Here we present the

EPTC-11. RURALITY INDEX SCORE AND PEDIATRIC NEURO-ONCOLOGICAL OUTCOME IN ONTARIO

Michelle Kameda-Smith, Gregory Pond, Forough Farrokhryan, and Hsien Seow; McMaster University, Hamilton, ON, Canada

Introduction: Rapid access to neurosurgical decisions and definitive management are vital for the outcome of neurocritical patients. There are inherent challenges of providing services to maintain critical care structure for rural citizens. The relationship between rurality, marginalization and health outcomes has been identified as associated with higher mortality rates and higher rates of many diseases[1]. Methods: Employing linked administrative databases, we retrospectively analyzed a population-based cohort of patients diagnosed with a pediatric brain tumour between 1996 to 2017 in Ontario, Canada. The Ontario Marginalization Index was employed as a surrogate for rurality providing an overall Rurality Index for Ontario (RIO) in addition to the 2016 Ontario Marginalization Index (ON-MARG). Results: Of 1457 patients included, 54.0% were male, 277 of whom were diagnosed in infancy (i.e., < 3 years of age). Income quintile was evenly distributed with 11.5% classified as living in a rural area of Ontario. The median[2] 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=0.092, median 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: Rulality 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 Alsoueih4, Ayoub Daksson4, Oulufem Ajan1, Blake Yarascavitch3, Adam Fleming3, Vivek Mehta4, Forough Farrokhryan2, Ali Yukilmaz2, Nina Steni3, and Sheila Singhi1; 1McMaster University, Hamilton, ON, Canada, 2University of Alberta, Edmonton, AB, Canada, 3University of Calgary, Calgary, AB, Canada, 4Dalhouse University, Halifax, NS, Canada

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.
results of subjects treated at dose level 1 (DL1; 1 million GD2-CAR T-cells/kg IV). Methods: Four patients (3 DIPG, 1 spinal DMG; ages 4–25; 1M/3F) were enrolled at DL1. Three subjects with H3K27M+ DIPG received 1e6 GD2-CAR T-cells/kg IV on study. One patient with spinal DMG enrolled but became ineligible after manufacturing and was treated on an eNd at DL1. An Omnimaya reservoir was placed in all subjects for therapeutic monitoring of intracranial pressure. Subjects underwent lymphodepletion with cyclophosphamide and thiotepa followed by GD2-CAR T cells 72 hours later for two weeks post-infusion. Results: All subjects developed cytokine release syndrome (Grade 1–3) manifested by fever, tachycardia and hypotension. Other toxicities included ICANS (Grade 1–2) and neurological symptoms/signs mediated by intratamor inflammation which we termed Tumor Immune-Affiliation-Associated Neurotoxicity (TIAN). No evidence of on-target off-tumor toxicity was observed in any patients. No dose-limiting toxicities occurred. CAR T cells trafficked to the CNS and were detected in CSF and blood. 3/4 patients exhibited marked improvement or resolution of neuro- logical deficits and radiographic improvement. The patient treated on an eNd exhibited >90% reduction in spinal DMG volume but progressed by month 3. Re-treatment of this subject via intracerebroventricular administration resulted in a second reduction in spinal DMG volume by ~80%. Conclusions: GD2-CAR T-cells at DL1 demonstrate a tolerable safety profile in patients with H3K27M+ DIPG/DMG with clear signs of T-cell expansion and activity including clinical responses.

EPC1-15. RAPID EPGENOMIC CLASSIFICATION OF BRAIN TUMORS ENABLES INTRAOPERATIVE NEUROSURGICAL RISK MODULATION

Luna Durakovic1, Skarphedinn Halldorsson1, Pett Niehusmann1,2, Henning Leske2,3, Luis P. Kuschel4, Jens Pahnek2,5, Bernt J. Due-Tønnessen1, Iver A. Langmoen4,6, Cecile J. Sandberg1, Philipp Euskirchen7, Emir O. Vik-Mo1,4, Wilhelm Magnus Laboratory for Neurosurgical Research, Institute for Surgical Research/ Department of Neurosurgery, Oslo University Hospital, Oslo, Norway, 2Section of Neuropathology, Department of Pathology, Oslo University Hospital, Oslo, Norway, 3Institute of Clinical Medicine (KlinMED), Faculty of Medicine, University of Oslo, Oslo, Norway, 4Department of Pathology, Berlin, Germany, 5Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia, 6Department of Neurosurgery, Oslo University Hospital, Oslo, Norway, 7German Cancer Consortium (DKTK), partner site Berlin, German Cancer Research Center (DKFZ), Berlin, Germany

Background: Clear identification of tumor subtype is the main predictor of patient outcome and ultimately what is considered an adequate level of surgical risk. At brain tumor resection, imaging modalities and intraoperative histology often give an ambiguous diagnosis, complicating intraoperative surgical decision-making. Here, we report a nanopore DNA methylation analysis (NDMA) sequencing approach combined with a machine learning algorithm for classification of candidate entities that could be used intraoperatively. Methods: We analyzed 50 biopsy samples from biobanked tissue (43, prospective) or sampled at surgery (7, intraoperative) for DNA methylation analysis. DNA was isolated from snap-frozen tissue samples using QIAamp DNA Mini Kit (Qiagen), quality assessed for purity using NanoDrop spectrophotometer. DNA was then barcoded with the Rapid Barcoding kit from Oxford Nanopore technologies and loaded onto a MinION flow cell. Sequencing was performed for 3 hours (intraoperative) and 24 hours (prospective). Raw reads were basecalled using the Guppy algorithm, then fed into a snakemake workflow (nanoDx - (intraoperative) and 24 hours (prospective). Raw reads were basecalled using the Guppy algorithm, then fed into a snakemake workflow (nanoDx - MODULATION

EPC1-17. DEVELOPING EYA PHOSPHATASE INHIBITORS WITH ON-TARGET EFFECTS IN SHH-MEDULLOBLASTOMA

Grace H. Hwang1,2, David A. Scott3, and Rosalind A. Segal1,2,1Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, MA, USA, 2Department of Biology, Harvard Medical School, Boston, MA, USA, 3Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, USA

Medulloblastoma, one of the most frequent malignant pediatric brain tumors, encompasses four molecularly and clinically distinct cancers. Sonic hedgehog (SHH)-subtype medulloblastoma constitutes about 30% of medulloblastomas, and therapies targeting the SHH pathway can lead to new highly selective treatment. The halothane dehalogenase (HAD) phosphatase Eyes Absent 1 (EYA1) is critically involved in the development and progression of SHH-medulloblastomas: Eya1 is highly expressed in SHH-medulloblastomas, and single cell sequencing indicates that Eya1 is a consistent feature that can be detected in every individual cancer cell. Inhibition of EYA1 interrupts the SHH pathway signaling. During normal development, EYA1 promotes symmetric division of cerebellar granule cell precursors (GCPs), the cells of origin for SHH-subtype medulloblastoma, and reduced levels of EYA1 decrease medulloblastoma mortality rates in mouse models. Therefore, targeting EYA1 may be a novel therapeutic avenue for these pediatric cancers. Benzamide derivatives have been suggested as allosteric EYA-inhibitors, and benzamide provides a promising platform for chemical derivatives. Here, we develop novel benzamide derivatives with higher affinity and higher selectivity for inhibiting SHH-medulloblastoma growth through the inhibition of EYA1. Several of the new compounds inhibit EYA1 phosphoryosine phosphatase activity in a cell-based assay, interrupt SHH pathway, and prevent SHH-medulloblastoma growth in vitro. Our results show that these novel benzamide derivatives are a new promising avenue for developing therapeutics for pediatric SHH-medulloblastoma via inhibition of EYA phosphatases.

EPC1-18. A TWO-PART, PHASE 1 STUDY OF RHEUMIN-186 NANOLIPOSOME (186RNL) DELIVERED BY CONVECTION ENHANCED DELIVERY FOR RECURRENT, REFRACTORY, OR PROGRESSIVE EPENDYMOMA AND HIGH-GRADE GLIOMA (HGG) AND NEWLY DIAGNOSED DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)

Ashley Plant1,2, Stewart Goldman1,4, Sandi Lani3,1, Michael DeCreppey1,2, Gregory Stein4, and Andrew Brenner3,4; Ann and Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, USA, 2Northwestern University Feinberg School of Medicine, Chicago, IL, USA, 3Phoenix Children’s Hospital, Phoenix, AZ, USA, 4University of Arizona College of Medicine, Phoenix, AZ, USA, 5Plus Therapeutics, Inc, Austin, TX, USA, 6University of Texas Health Science at San Antonio, San Antonio, TX, USA

Ependymoma, HGG, and DIPG are gliomas that are often difficult to treat, frequently aggressive, and often carry an extremely poor prognosis. While external beam radiation therapy (EBRT) remains a central component of