Lake City, UT, USA, [7]Department of Pediatrics, University of Utah, Salt Lake City, UT, USA

Background: CNS tumors are the most common solid tumors and the deadliest cancers in children. Approximately 10% of children with a CNS tumor harbor a hereditary cancer syndrome (HCS), but many will not be tested for a HCS. The Utah Population Database (UPDB) contains comprehensive cancer registry data for Utah families and can determine multigenerational cancer pedigrees across an archive of 5.8 million individuals. We hypothesize that the UPDB can identify children and families with HCSs not previously identified. Methods: We queried the UPDB for individuals ages 0–39 diagnosed with a primary CNS tumor (malignant and benign) between 1966–2017 and generated cancer pedigrees of 3 generations or more for probands, extending to at least third-degree relatives. Specialized software calculated a familial standardized incidence ratio (FSIR) to determine families with excess clustering of CNS tumors. Clinical cancer genetics experts reviewed pedigrees to confirm patterns of HCS. Results: We identified 4,634 CNS tumors in 4,550 individuals, of whom 2,233 (49%) reside in high-quality pedigrees containing ≥2 grandparents, at least 1 from both maternal and paternal sides. To identify families with excess clustering of CNS tumors, we selected pedigrees with an FSIR $P<0.05$ and ≥2 affected patients, resulting in 161 high-risk families with a mean of 170 (median 96) relatives per pedigree of 3–6 generations. Among these 161 families, there were 2,017 unique relatives (first-third degree) of CNS probands with 2,355 tumors (any site), for a per pedigree average of 14.7 tumors in 12.5 relatives. Review of the 10 highest risk pedigrees indicated that 4 meet HCS criteria, including Li-Fraumeni (n=2), von Hippel-Lindau (n=1), and rhabdoid tumor predisposition (n=1). Conclusion: The UPDB can produce multigenerational cancer pedigrees that identify individuals and families at risk of harboring a HCS who warrant germline testing. These findings should encourage clinicians to perform thorough family history screening.

RARE-25. DISSECTING THE CONTEMPORARY EPIDEMIOLOGY OF PRIMARY AND SECONDARY BRAIN TUMORS IN INFANCY THROUGH CHILDHOOD

Nayan Lamba[1] and Bryan Iorgulescu[2,3]; [1]Massachusetts General Hospital, Boston, MA, USA, [2]Dana-Farber Cancer Institute, Boston, MA, USA, [3]Brigham and Women's Hospital, Boston, MA, USA

Introduction: Herein we utilize national registry data to evaluate the epidemiology of primary and secondary pediatric brain tumors according to the WHO2016 classification. Methods: Pediatric patients (age≤14) presenting between 2004–2017 with a brain tumor were identified by ICD-O-3 and brain metastasis (2010–2017) coding from the National Cancer Database (comprising >70% of newly-diagnosed cancers in the U.S.), and categorized by NICHD age stages: infant (<1yr; n=1,686), toddler (1-2yrs; n=1,732), early- (2-5yrs; n=6,712), middle- (6-11yrs; n=9,175), and late- (12-14yrs; n=5,042) childhood. Patients' age, sex, race/ethnicity, and overall survival, and tumor location and size were evaluated by WHO2016 tumor type. Results: 24,347 pediatric brain tumor patients were identified. Overall, other astrocytic tumors (24% of females, 20% of males), diffuse astrocytic/oligodendroglial gliomas (23% of females, 21% of males – 64% of which were midline), embryonal (13% of females, 19% of males), and sellar region tumors (12% of females, 8% of males) predominated. Embryonal tumors prevailed in infancy (24%) and toddlerhood (24%), declining to 9% in late childhood; only 40% were female. Ependymal tumors peaked at 15% in toddlerhood (6% overall), whereas choroid plexus tumors peaked at 11% in infancy (1.9% overall). A minority of brain tumors were of neuronal & mixed neuronal-glial (6.1%), germ cell (3.8%), cranial nerve (3.2%), mesenchymal non-meningothelial (2.4%), meningioma (1.6%), pineal (1.1%), hematological/histiocytic (0.5%), and other glioma (0.2%) types. Brain metastases were rare (1.5% overall; from 4.0% in infancy to 0.8% in late childhood; and only 41% were female) – 61% came from adrenal neuroblastoma, 16% from sarcomas, and 6% from malignant rhabdoid tumors/extracranial AT/RT. Conclusions: Pediatric brain metastases overwhelmingly originate from adrenal neuroblastoma. Although, overall, diffuse astrocytic/oligodendroglial, other astrocytic, embryonal, and sellar region tumors predominate among pediatric brain tumors, together they only comprise 70% of cases and their distribution varies substantially by patients' age and sex.

TRANSLATIONAL/EARLY PHASE CLINICAL TRIALS

EPCT-01. A NOVEL PEPTIDE VACCINE DIRECTED TO CMV PP65 FOR TREATMENT OF RECURRENT MALIGNANT GLIOMA AND MEDULLOBLASTOMA IN CHILDREN AND YOUNG ADULTS: PRELIMINARY RESULTS OF A PHASE I TRIAL

Eric Thompson[1], Daniel Landi[1], Gerald Archer[1], Eric Lipp[1], Ashley Walter[1], Bridget Archambault[1], Bea Balajonda[1], Charlene Flahiff[1], Denise Jaggers[1], James Herndon[1], Evan Buckley[1], Kristin Schroeder[1], Dina Randazzo[1], Annick Desjardins[1], Margaret Johnson[1], Katherine Peters[1], Mustafa Khasraw[1], Michael Malinzak[1], Duane Michell[2], David Ashley[1], and John Sampson[1]; [1]Duke University, Durham, NC, USA, [2]University of Florida, Gainesville, FL, USA

Introduction: The cytomegalovirus (CMV) antigen, pp65, is ubiquitously expressed in malignant glioma and medulloblastoma but not in healthy brain. The objective of this Phase I trial (NCT03299309) was to assess the safety and feasibility of a novel pp65 peptide vaccine (PEP-CMV) in children and young adults with recurrent medulloblastoma and malignant glioma. Methods: Vaccines contain a synthetic long peptide (SLP) of 26 amino acids encoding multiple potential class I, class II, and antibody epitopes of CMV pp65 across several haplotypes. This SLP is administered as an emulsion in Montanide ISA 51. Patients receive a single course of temozolomide to induce lymphopenia, tetanus/diphtheria toxoid site preconditioning, then vaccines administered intradermally every two weeks for 3 doses, then monthly. Results: To date, 22 patients have been enrolled. Diagnoses include medulloblastoma (n=2), glioblastoma (n=12), anaplastic oligodendroglioma (n=2), anaplastic astrocytoma (n=3), and malignant glioma NOS (n=3). Mean number of prior treatment regimens is 4.9 (range 1–12). Mean age is 22yo (range 6–35) and 45% of patients are male. The median KPS is 80. The median number of vaccines given at time of analysis is 3.3 (range 1–12). There have been no ≥ 3 Grade toxicities related to the vaccine. One patient developed nausea, vomiting, palpitations, and tachycardia after vaccination and had elevated inflammatory cytokines consistent with cytokine release syndrome. Median PFS is 2.5 months (95% CI: 1.7,4.5) and median OS is 6.5 months (95% CI 3.3, 7.9). Immune response to pp65 as determined by ELISpot was found in 75% of patients. On MRI 6 of the 11 evaluable patients have had at least stable disease with three of those having a partial response. Conclusions: Preliminary results demonstrate that PEP-CMV is well-tolerated and elicits an immune response in heavily pretreated, multiply recurrent patients. A multi-institutional Phase II trial is scheduled to open fall 2021.

EPCT-02. COMPARISON OF TARGETED AGENTS RECOMMENDED BY THE CNS-TAP TOOL TO THOSE SELECTED BY A TUMOR BOARD IN A MOLECULARLY-DRIVEN DIPG CLINICAL TRIAL

Holly Roberts[1], Karthik Ravi[1], Bernard Marini[1,2], Cassie Kline[3,4], Sabine Mueller[5], Carl Koschmann[1], and Andrea Franson[1]; [1]University of Michigan Medical School, Ann Arbor, MI, USA, [2]Department of Clinical Pharmacy and Pharmacy Services, University of Michigan, Ann Arbor, MI, USA, [3]Children's Hospital of Philadelphia, Philadelphia, PA, USA, [4]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [5]School of Medicine, University of California, San Francisco, San Francisco, CA, USA

Recently, sequencing of diffuse intrinsic pontine glioma (DIPG) biopsy specimens has revealed genomic heterogeneity of these tumors, fueling an interest in individualized, targeted treatment options. The Pacific Pediatric Neuro-Oncology Consortium recently completed enrollment onto a feasibility study PNOC003: Molecular Profiling for Individualized Treatment Plan for DIPG (NCT02274987), in which a multidisciplinary tumor board recommended molecularly-targeted agents based on genomic and molecular profiling of each patient's tumor. Separately, our group developed the Central Nervous System Targeted Agent Prediction (CNS-TAP) tool, which combines pre-clinical, clinical, and CNS penetration data with patient-specific genomic information to allow for numeric scoring of targeted anticancer agents to objectively evaluate these therapies for use in patients with CNS tumors. We hypothesized that highly-scored agents within CNS-TAP would overlap with the agents recommended by the tumor board in this study. For each PNOC003 participant, we utilized the genomic report to identify actionable alterations and input patient-specific data into CNS-TAP to identify the highest scoring agents. We compared high-scoring agents within CNS-TAP with recommendations from the PNOC003 tumor board for each of the enrolled 28 subjects. Overall, 93% (26/28) of patients had at least one agent recommended by both the tumor board and CNS-TAP. Additionally, 38% (37/95) of all agents recommended by the tumor board were also selected by CNS-TAP. Furthermore, we identified factors that likely contributed to the discordance between these two methods. Without clinician input, CNS-TAP is unable to account for drug-drug interactions, includes only designated anticancer agents, and cannot easily be updated in real time. However, CNS-TAP provides an objective evaluation of targeted therapies, whereas tumor boards are inherently subjective. Given the discordance identified between these methods and the strengths of each, a prospective study incorporating both CNS-TAP and a molecular tumor board for targeted therapy selection in DIPG patients is warranted.

EPCT-03. SERIAL PLASMA AND CSF CELL-FREE TUMOR DNA (CF-TDNA) TRACKING IN DIFFUSE MIDLINE GLIOMA PATIENTS UNDERGOING TREATMENT WITH ONC201

Evan Cantor[1], Kyle Wierzbicki[1], Rohinton S. Tarapore[2], Chase Thomas[1], Rodrigo Cartaxo[1], Viveka Nand Yadav[1], Ramya Ravindran[1],