parties have been developed but not utilized prospectively in children with central nervous system tumors (CNS). OBJECTIVE: To establish a baseline assessment of health-related quality of life and associated social determinants of health in children diagnosed with CNS tumors in Indiana. METHOD: We implemented the Pediatric Quality of Life Inventory® (PedsQL™) for patients (ages 0-21 years) diagnosed with a CNS tumor evaluated in the neuro-oncology clinic from July 2019-January 2022. A higher score is associated with a better perception of quality of life. Patient’s overall Quality of Life (QOL) was assessed by the Total Parent/Observer Form (30 items), and the Total Child Form (33 items). RESULTS: We assessed 107 patients and their parents. The median age at diagnosis was 6 years (min 0.4; max 19.2) years. The median age at assessment was 4.5 years (min 0.4; max 14.8) years. Parents (n=77) had a median of 12 years of education (min 0; max 24). The PedsQL™ was completed by 96 parents and 91 patients. Physical mean was 67.4 and 71.2, psychosocial mean 67.8 ± 6.9, and total mean 67.7 ± 6.9, respectively. Simple linear regressions demonstrated a correlation between increasing disparity and decreasing quality of life across all dimensions. CONCLUSION: This is one of the studies to associate a decrease in pediatric quality of life with disparities of social determinants of health. This data demonstrate the need for expanded prospective evaluation to track social determinants of health that may impact on the quality of life in children diagnosed with CNS tumors.

OTHR-36. MANAGEMENT OF CENTRAL DIABETES INSIPIDUS (CDI) WITH LOW-DOSE VASOPRESSIN INFUSION IN PATIENTS WITH NON-GERMINOMATOUS GERM CELL TUMORS (NGGCT) REQUIRING HYPERHYDRATION DURING CHEMOTHERAPY

Caroline Fitzgerald, Kathryn Matson; Boston Children's Hospital, Boston, MA, USA

Primary intracranial germ cell tumors (GCT) represent 3-5% of central nervous system tumors with non-germinomatous germ cell tumors (NGGCTs) comprising approximately one-third. Located in the pineal and suprasellar regions, the tumors can cause central diabetes insipidus (CDI). Induction chemotherapy for NGGCT includes ifosfamide. Due to the risk of hemorrhagic cysts associated with ifosfamide, 3000 mL/m2/day of intravenous fluids is administered. Oral desmopressin (DDAVP), the mainstay of treatment for CDI, has a long duration of action, variable intensity and can lead to hyponatremia and water intoxication due to the retention of large quantities of free water. Therefore, DDAVP is held during hyperhydration resulting in significant diuresis leading to patient discomfort and increased risk for wide electrolyte fluctuations. The volume of dextrose-containing IV fluids also places patients at risk for hyperglycemia and other metabolic disturbances. Patients with NGGCTs and CDI at our institution are admitted to the ICU for ifosfamide cycles due to the need for close monitoring and potential IV access. ICU admission delays and potentially places patients in a setting where staff are unfamiliar with chemotherapy administration, increasing the risk of safety-related events. From a cost, resource, and patient care perspective, these admissions are suboptimal. This prompted a search for evidence to maintain patients safely out of the ICU. A literature search provided case studies citing the use of low-dose IV vasopressin. In collaboration with our endocrine and pharmacy colleagues we prompted a search for evidence to maintain patients safely out of the ICU. Source, and patient care perspective, these admissions are suboptimal. This is important to inform the patients and their guardians of the potential cutaneous toxicities prior to treatment initiation, and to refer them to a dermatologist for proper management.

OTHR-38. THE DEVELOPMENT OF PATIENT-DERIVED MODELS OF PEDIATRIC BRAIN TUMORS

Julie Messina1,2, Marleen Derweduwe1, Annelies Claey3, Lien Slienz3,4, Raf Sciot1,4, Isabelle Vanden Bemt5,6, Steven Devleeschouwer1,4, Frank Van Calenbergh1, Philippe De Vloo7, Bart Depreitere1,2, Sande Jacobs6,7, Frederik Depretere8, 1Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium. 2Laboratory for Precision Cancer Medicine, Translational Cell- and Tissue Research, Department of Imaging and Pathology, KU Leuven, Leuven, Belgium. 3Research Group Experimental and Neuro-Oncology, Department of Neurosciences, KU Leuven, Leuven, Belgium. 4Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium. 5Translational Cell- and Tissue Research, Department of Imaging and Pathology, KU Leuven, Leuven, Belgium. 6Department of Neuro-Oncology, University Hospitals Leuven, Leuven, Belgium. 7Department of Human Genetics, University Hospitals Leuven, Leuven, Belgium. 8Department of Human Genetics, KU Leuven, Leuven, Belgium. 9Department of Pediatric Hematology and Oncology, Department of Pediatrics, University Hospitals Leuven, Leuven, Belgium. 10Department of Pediatric Oncology, KU Leuven, Leuven, Belgium.

Brain tumors are still a major cause of morbidity and mortality in children, despite extensive research. An individualized therapy is warranted to combat the heterogeneity present in these tumors. Therefore, this study aims at developing patient-derived models from both low- and high-grade tumors. As such, the heterogeneity of these tumors can be further characterized and treatment sensitivities can be studied. All pediatric patients diagnosed with a brain tumor at the University Hospitals Leuven and receiving surgical intervention were included after informed consent. If sufficient tumoral material was available, a fresh tumor sample was collected during surgery. The sample was processed into dissectible cells, which were grown in culture in order to develop a patient-derived cell line (PDCI). Bio-marker expression using a qPCR array was performed if growth beyond passage 3 was achieved. Established PDCIs were subsequently subjected to genomic and transcriptional profiling and cytotoxicity assays were performed to determine therapeutic sensitivities. Patient-derived xenografts (PDX) are developed in selected cases. 70 patients were included prospectively up until January 2022 and tumoral material was available for 50 of them. In total, 10 PDCIs could be generated (3 high-grade, 7 low-grade, 3 NGGCTs), while 9 early cultures (3 high-grade, 6 low-grade) are still being expanded. qPCR and sequencing analysis confirm preservation of driving mutations. The high level of growth failures of the PDCIs can be explained by the high proportion of lower grade tumors included. One PDX model was generated. In conclusion, novel patient-derived models from pediatric brain tumors have been generated, which recapitulate the characteristics of the original tumor. The models are a valuable tool to study these tumors and the responses to different treatments. Further on, we will continue with the development of these models and the study of their therapeutic sensitivities.

OTHR-39. EXTRANEURAL SPREADING OF A DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR IN A CHILD: PATIENT-DERIVED MODELS SHOW SENSITIVITY TO VINBLASTIN AND TRAMETINIB

Julie Messina1,2, Annelies Claey3, Aniek Shety3, Lien Spaen4, Marleen Derweduwe1, Anne Uytebroek5, Bart Depreitere1,4, Isabelle Vanden Bemt5,6, Raf Sciot1,4, Keith Ligon6,8, David Jones6,11, Caroline Fitzgerald, Kathryn Matson; Boston Children’s Hospital, Boston, MA, USA

Objective: To describe the cutaneous adverse effects (AE) to MAPK Extracellular Signal-Regulated Kinase Inhibitor Trametinib in the pediatric population. METHODS: This was a retrospective single-center study. Included were all pediatric patients, treated with trametinib, for an oncologic indication. All patients were evaluated by a pediatric dermatologist, prior to, and during treatment, with documentation of cutaneous findings. Treatment was started at 0.375 mg/m2/day (n=6); trametinib was reduced to 0.25 mg/m2/day (n=1); trametinib was discontinued (n=1). AE were documented and assessed. RESULTS: 7 patients received treatment with trametinib, of which 6 received a combination of trametinib and dabrafenib (BRAF inhibitor). Out of twenty patients, 18 patients (90%) presented with at least one cutaneous AE. Xerosis and pruritic eczematous changes were the most common (15 patients, 73%), which, in most cases, were tolerable and responded well to the use of emollients and topical corticosteroids. Eleven patients (55%) presented with paronychia which was treated with topical combined corticosteroids antifungals and antibiotics, all with good response. Six patients (30%) presented with reversible hair heterochromia, treated with topical tretinoin, mostly with good response. Six patients (30%) presented with reversible hair heterochromia. Reaction grades were reported for cutaneous reactions, most of them were Grade I or II. Only 2 patients reported to have grade III or IV cutaneous reactions. Dabrafenib was utilized in cases of desquamative and erythema multiforme, respectively. Out of 6 patients that received combined treatment of trametinib and dabrafenib one patient had no cutaneous adverse reaction, and one had panannulitis (which was related to dabrafenib). The rest presented relatively mild AE. DISCUSSION: Cutaneous AEs are very common in children and adolescents treated with trametinib, and in most cases are classified as mild. Nevertheless, as this treatment is usually chronic, it is important to inform the patients and their guardians of the potential cutaneous toxicities prior to treatment initiation, and to refer them to a dermatologist for proper management.
Oncology, KU Leuven, Leuven, Belgium.  2Department of Pediatric Hematology Oncology, Department of Pediatrics, University Hospitals Leuven, Leuven, Belgium.  3Research Group Experimental Neurosurgery and Neuroanatomy, University Hospitals Leuven, Leuven, Belgium.  4Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium.  5Department of Human Genetics, KU Leuven, Leuven, Belgium.  6Translational Cell and Tissue Research, Department of Imaging and Pathology, KU Leuven, Leuven, Belgium.  7Department of Surgery, University of Manchester, Manchester, United Kingdom.  8Department of Oncologic Pathology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA.  9Hopp Children’s Cancer Center at the NCT Heidelberg (KiTZ), Heidelberg, Germany.  10Division of Pediatric Neurooncology, German Cancer Consortium (DKTK), German Cancer Research Group Center (DKFZ), Heidelberg, Germany.

Leptomeningeal glioneuronal tumors (DLGNT) are rare neoplasms of the central nervous system. We describe the generation of patient-derived models of a DLGNT that metastasized to the peritoneal cavity via a ventriculoperitoneal shunt in a child. The original tumor contained a KIAA1349:BRAF fusion with a chromosome 1p deletion and corresponded with metastasis subclass DLGNT-MC-2. From a sample of ascitic fluid, metastatic tumor cells could be extracted and expanded ex vivo into a long-term cell culture model. This patient-derived cell line (PDCL) showed mixed morphological phenotypes and expressed MAP2 and SYP. The KIAA1349:BRAF fusion was preserved and the PDCL still corresponded to the original metastasis subclass DLGNT-MC-2. Whole-genome sequencing showed additional mutations potentially contributing to the malignant behavior of the tumor. Cytotoxic assays performed on the PDCL indicated high sensitivity to vinblastine and trametinib (MEK-inhibitor) and intermediate sensitivity to DRC/ClpP-modulators. A metastatic viral transduction to induce GFP-βLux positivity and was intraperitoneally injected into immunocompromised mice. A mouse model could be generated, with the growth of a peritoneal tumor in a localized manner. The cells grown from this metastatic mouse tumor were again put into culture and were subjected to the same treatments as the PDCL. This confirmed a similar profile, with high sensitivity to vinblastin and trametinib and an intermediate sensitivity to the DRC/ClpP-modulators. In conclusion, we were able to generate patient-derived models from a metastatic DLGNT, which recapitulate the molecular characteristics of the original tumor. The models showed high sensitivity to vinblastin and targeted therapy with MEK-inhibition, but further studies are necessary to define the adequate treatment for this kind of tumor.

OTHR-40. DICER 1- A RARE, BUT IMPORTANT TUMOR DRIVER IN MALIGNANT PROGRESSIVE BRAIN TUMORS

Jero Freij1, Laila Rosman1, Yael Fisher2, 1Sheba zedeek medical center, Jerusalem, Israel; 2zambam medical center, Jerusalem, Israel.

BACKGROUND: DICER mutation is a known tumor driver involved in pleuropneumonial blastoma (PnB, masses in the thyroid and ovary and metastasis to other organs). Brain tumors are not considered to be a rare manifestation of germline DICER mutation. Currently, brain imaging is not included in the standard follow up of patients with DICER germline mutation, and data regarding the prevalence of somatic DICER mutations in brain tumors is limited. AIMs: To evaluate the prevalence of DICER mutations in brain tumors, to evaluate sensitivity to DRC/ClpP-modulators. METHODS: The study included patients with brain tumors who were referred to our center for curative standard therapy in Israel were sent for next generation sequencing. MoDiSC was run in 438 patients with suspected brain tumors. In the subset of patients with DICER mutation, molecular evaluation was done using either panel based evaluation (ONCOMINE/INMORM) or whole exome and whole transcriptome (INFORM) consisting of patient DNA. RESULTS: From the original patients with a DICER mutation, 7 were subjected to the same treatments as the PDCL. This confirmed a similar profile, with high sensitivity to vinblastine and trametinib (MEK-inhibitor) and intermediate sensitivity to DRC/ClpP-modulators. In conclusion, we were able to generate patient-derived models from a metastatic DLGNT, which recapitulate the molecular characteristics of the original tumor. The models showed high sensitivity to vinblastin and targeted therapy with MEK-inhibition, but further studies are necessary to define the adequate treatment for this kind of tumor.

OTHR-41. AMPLIFICATION OF THE PLAG FAMILY GENES – PLAG1 AND PLAGL2 – IS A KEY FEATURE OF A NOVEL EMBRYONAL CNS TUMOR TYPE

Michaela-Kristina Keck1, 2, Martin Sill1, 3, Andrea Wittmann1, 2, Priyush Joshi Kumar1, 2, Damian Stichel1, 2, Philipp Sievers1, 2, Annika K. Weiters3, 4, Federico Roncaroli5, James Hayden1, 2, Martin G. McCabe2, 4, Mariette E. G. Kranendonk5, 6, Machal Zapotoczky1, 7, Alexandre Vasilevski1, 2, Ulrich Schüller6, 8, Dominik Sturm1, 2, Mirjam Blattner-Johnson1, 9, Andreas von Deimling5, 9, Andrey Kononenko1, 10, Felix Sahmi1, 10, Ana David Solomon1, 10, Stefan Pfitzer1, 10, David T.W. Jones1, 10, Jero Freij1, 2, Hopp Children’s Cancer Center Heidelberg (KiTZ), Heidelberg, Germany.  2Division of Pediatric Glioma Research, German Cancer Research Center (DKFZ), Heidelberg, Germany.  3Division of Pediatric Neurooncology, German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany.  4Department of Neuropathology, Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany.  5Clinical Cooperation Unit Neuropathology, German Consortium for Translational Cancer Research (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany.  6Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.  7Division of Neuroscience and Experimental Psychology, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom.  8Department of Pediatric Hematology and Oncology, Alder Hey Children’s NHS Foundation Trust, Liverpool, United Kingdom.  9Division of Cancer Sciences, University of Manchester, Manchester Academic Health Centre, Manchester, United Kingdom.  10Institute of Human Genetics, KU Leuven, Leuven, Belgium.  11Centre de Pathologie et Neuropathologie, Hospices Civils de Lyon, Lyon, France.  12Department of Pathology, Division of Neuropathology, University of California San Francisco (UCSF), San Francisco, USA.  13Department of Pathology and Department of Neurosurgical Surgery, Division of Neuropathology, University of California San Francisco (UCSF), San Francisco, USA.  14Division of Pediatric Neurooncology, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Pediatric central nervous system (CNS) tumors differ substantially from their adult counterparts, are marked by considerable molecular and clinical heterogeneity, and diagnosis through histopathology alone can be challenging. Using a novel approach of CNS tumor classification in combination with a newly developed copy number and RNAseq analysis, we identify a rare, novel pediatric CNS tumor type (n=32) which is characterized by focal high-level amplification and consecutive overexpression of one of the PLAG family genes – PLAG1 or PLGAL2, and whole genome sequencing (WGS) for other known tumor types such as high-grade gliomas, medulloblastomas, embryonal tumors, or CNS sarcomas. The wide range of original histopathologic diagnoses rendered attests to their polyphenotypic nature in terms of morphology. We suggest that these tumors may use a myeloid to intermediate neural progenitor cells with some neuronal commitment. Using ChIPseq data, we show that both PLAG1 and PLGAL2 act as transcription factors for: i) the oncogenic kinase RET, a potential drug target, that was overexpressed in our cohort; ii) components of the Wnt-β-Catenin pathway; iii) a set of imprinted genes, reported to mediate sensitivity to the DRD/ClpP-modulators. In conclusion, we were able to generate patient-derived models from a metastatic DLGNT, which recapitulate the molecular characteristics of the original tumor. The models showed high sensitivity to vinblastin and targeted therapy with MEK-inhibition, but further studies are necessary to define the adequate treatment for this kind of tumor.