parities 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 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 better quality of life. Patient's address was utilized to obtain Area Deprivation Index (ADI) and Child Opportunity Index (COI). ADI allows for rankings of neighborhoods by socioeconomic disadvantage at state or national level (1-10: 1 is least disadvantaged). COI measures the quality of resources in a patients' community, with five categories ranging from very low- to very high-opportunity. RESULTS: We assessed 107 patients and their parents. The ADI decile within Indiana ranged 1 to 10 (median 5, mean 5.3); national percentile ranged 7 to 100 (median 71, mean 67.3). Overall COI mean was 3, with sub-scores for education - 2.9, health/environment - 2.6, and social/economic - 3.1. The PedsQL™ was completed by 96 parents and 91 patients. Physical mean was 67.4 and 71.2, psychosocial mean 67.8, 68.9, and total mean 67.7, 69.8, respectively. Simple linear regressions demonstrated a correlation between increasing disparity and decreasing quality of life across all dimensions. CONCLUSION: This is one of the first studies to associate a decrease in pediatric quality of life with disparities of social determinants of health. These 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

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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 cystitis 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 prompt interventions. ICU admission can delay therapy 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 created a protocol to treat patients with CDI receiving chemotherapy with hyperhydration with a low-dose, easily titratable intravenous vasopressin infusion, to keep urine mildly diluted to allow enough diuresis to decrease injury while preventing excessive fluid losses and wide variations in electrolytes.

OTHR-37. PEDIATRICS CUTANEOUS REACTIONS IN PATIENT TREATED WITH THE MITOGEN-ACTIVATED PROTEIN KINASE EXTRACELLULAR SIGNAL-REGULATED KINASE INHIBITOR TRAMETINIB

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OBJECTIVE: To describe the cutaneous adverse effects (AE) to MAPK Extracellular Signal-Regulated Kinase (MEK) 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. RESULT: Twenty patients were enrolled in the study. All 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, 75%), 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 acneiform eruption, treated with topical antibiotic, benzoyl peroxide and tretinoin, mostly with good response. Six patients (30%) presented with irreversible 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 and IV cutaneous reactions: exfoliative dermatitis 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 panniculitis (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.

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

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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 in 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 dissociated cells, which were grown in culture in order to develop a patient-derived cell line (PDCL). Biomarker expression using a qPCR array was performed if growth beyond passage 3 was achieved. Established PDCLs were subsequently subjected to genomic and transcriptional profiling and cytotoxicity assays were performed to determine therapeutic sensitivities. Patient-derived xenografts (PDX) are developped in selected cases. 70 patients were included prospectively up until January 2022 and tumoral material was available for 50 of them. In total, 10 PDCLs could be generated (3 high-grade, 7 low-grade tumors), 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 PDCLs 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. This will help further improving the understanding of these tumors.

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

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Diffuse leptomeningeal glioneuronal tumors (DLGNT) are rare neoplasms of the central nervous system. We describe the generation of patient-derived models from a DLGNT that metastasized to the peritoneal cavity via a ventriculoperitoneal shunt in a child. The original tumor contained a KIAA1549:BRAF fusion with a chromosome 1p deletion and corresponded with methylation subclass DLGNT-MC-2 From a sample of ascitic fluid, metastatic tumoral 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 KIAA1549:BRAF fusion was preserved and the PDCL still corresponded to the original methylation 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 DRD/ClpP-modulators. The PDCL underwent viral transduction to induce GFP-fLux 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 the mouse tumor were again put into culture and were afterwards 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 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.

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

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BACKGROUND: DICER mutation is a known tumor driver involved in pleuropulmonary blastoma ,renal tumors, masses in the thyroid and ovary and multiple other manifestations. Brain tumors are 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 re the prevalence of somatic DICER mutations in brain tumors is limited. AIMs: evaluation of prevalence of DICER mutations in a large cohort of rare/relapsed brain tumors. METHODS: over the last year all patients with tumors lacking curative standard therapy in Israel were sent for next generation sequencing,. Molecular evaluation was done using either panel based evaluation (ONCOMINE/ Foundation) or whole exome and whole transcriptome (INFORM consortium). Epidemiological data as well as clinical outcome were provided by the treating physician. RESULTS: Between April 2021 and January 2022 one hundred twenty nine samples were sent for molecular analysis, 58 of them were brain tumors. Six patients had DICER associated malignant tumors , 33% of them were brain tumors . One patient with pinealoblastoma was diagnosed with a highly metastatic disease associated with a very grave prognosis. CONCLUSION: brain tumors are an important group among malignant DICER associated tumors. Surveillance may lead to early detection which may be associated with a better outcome.

OTHR-41. AMPLIFICATION OF THE PLAG FAMILY GENES – PLAGL1 AND PLAGL2 – IS A KEY FEATURE OF A NOVEL EMBRYONAL CNS TUMOR TYPE

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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 DNA methylation-based CNS tumor classification in combination with 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 – PLAGL1 or PLAGL2. It is epigenetically divergent from other known tumor types such as high-grade gliomas, medulloblastomas, embryonal tumors, or CNS sarcomas. The wide range of original histopathologic diagnosis rendered attests to their polyphenotypic nature in terms of morphology. We suggest that these tumors may arise from early to intermediate neural progenitor cells with some neuronal commitment. Using ChIPseq data, we show that both PLAGL1 and PLAGL2 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 regulate the imprinted gene network in mouse models, that was deregulated in the PLAGL-amplified tumors. Consequently, a 250-gene expression PLAGL-signature indicated dysregulation of imprinting control and differentiation/development as a prominent feature. We report differences regarding age and sex distribution between PLAGL1- and PLAGL2-amplified tumors and shed light on differences in clinical behavior and outcomes between these subtypes in male and female patients. PLAGL1-amplified tumors were more prevalent in school-age children and teenagers, while PLAGL2-amplified cases occurred in very young patients. Kaplan-Meier analysis showed a trend towards a more favorable outcome in patients with PLAGL1-amplified tumors and in female patients. Survival rates remained constant after 5 years with a five-/ten-year overall survival of 75% for PLAGL1, 24% for PLAGL2, 18% for male patients, and 88% for female patients.

OTHR-42. MISSING DATA TOLERANT INTEGRATION OF PROTEOMIC DATASETS ENABLES THE IDENTIFICATION AND CHARACTERIZATION OF BRAIN CANCER SUBTYPES

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Investigating the proteome can add a significant layer of information to manifold existing methylation, mutation, and transcriptome data on brain tumors as proteins represent the pharmacologically addressable phenotype of a disease. Small cohorts limit the usability and validity of statistical methods, and variable technical setups and high numbers of missing values make data integration from public sources challenging. Using a newly developed framework being able to reduce batch effects without the need for data reduction or missing value imputation, we show –based on in-house and publicly available datasets- successful integration of proteomic data across different tissue types, quantification platforms, and technical setups. Exemplarily, data of a Sonic hedgehog (Shh) medulloblastoma mouse model were analyzed, showing efficient data integration independent of tissue preservation strategy or batch. We further integrated batches of publicly available data of human brain tumors, confirming proposed proteomic cancer subtypes correlating with clinical features. We show that, missing value tolerant reduction of technical variances may be helpful to identify biomarkers, proteomic signatures, and altered pathways characteristic for molecular brain cancer subtypes.