RAF inhibitor (one), and combination MEK-mTOR inhibition (one). Six have completed the three-month follow-up. Of these six, four rated their satisfaction with the kit as excellent, one each rated very good and fair satisfaction. Five participants rated the kit helpful and thought the kits should be distributed when patients begin therapy. Three started taking their targeted agent before enrolling in the study and their CDLQI changed from 3 to 0.3 (means; improved). Three participants started their targeted agent after enrollment and their CDLQI changed from 1 to 3.3 (means; worsened). CONCLUSIONS: Participants reported that skin care kits were helpful and recommended use by other patients on MAPK-targeted agents. Continued follow-up and enrollment in the study will help further explore the utility of specific products in the kits, as well as changes in patients' QOL.

**OTHR-19. DISORDERED CELL MIGRATION IN THE CEREBRAL CORTEX CAUSED BY LIN28A OVEREXPRESSION AND WNT PATHWAY ACTIVATION IN NEURAL PRECURSOR CELLS**

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LIN28A overexpression and mutations of the Wnt pathway gene *CTNNB1* have been described in rare malignant brain tumors of early childhood. In order to investigate the interplay of the oncogenic proteins Lin28A and Ctnnb1 during embryonal brain development, we overexpressed these components in neural progenitor cells in vivo. The sole overexpression of either Lin28A, stabilized Ctnnb1 (*Ctnnb1Δex3*) or the combination of both in hGFAP-positive forebrain precursor cells did not lead to brain tumor formation but resulted in distinct phenotypes in the cerebral cortex during embryonal development. The *hGFAP-cre::IsI-Lin28A* (GL) mouse model showed transiently increased proliferation in the cerebral ventricular zone and proper isocortical layering. *hGFAP-cre::Ctnnb1Δex3fl/+* (GB) and *hGFAP-cre::Ctnnb1Δex3fl/+::IsI-Lin28A* (GBL) mice developed a hydrocephalus and showed disturbed cortical layering. GB mice displayed cerebral hypoplasia with a thinned cortex, while the GBL cortices showed variable thickness. Immunostainings with the pial marker Laminin and dendritic marker Map2c revealed a porous pia mater and aggregations of neurons above the pial border in the GBL model at embryonal day 14 (E14.5). At later embryonal stage (E18.5), the GBL model showed also large blood vessels located in deeper cortical layers. Proteome analyses of GB and GBL cortices revealed decreased abundance of the Lissencephaly associated component Reelin-receptor Lrp8 compared to *hGFAP-cre* control mice. Additionally, we found 92 proteins, which were altered specifically in the GBL mouse model. These results indicate that the co-expression of Lin28A and *Ctnnb1Δex3* in neural precursor cells does not lead to brain tumor formation but results in neuronal migration disturbances with ectopic neurons in the subarachnoid area. Whereas the GB phenotype is reminiscent of human lissencephaly type I, GBL brain morphology showed similarities to neuronal overmigration observed in the migration disorder of human Cobblestone (Type II) Lissencephaly.

**OTHR-20. PRECISION NEURO-ONCOLOGY IN THE REAL WORLD. OPPORTUNITY AND CHALLENGES FROM A UK ONCOLOGY CENTRE**

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The last five years has shown advances in the molecular classification of brain tumour, molecular profiling techniques and an increased use of targeted therapies. We reviewed the molecular analysis pathways and use of targeted agents at Birmingham Children's Hospital (BCH), a large (~55 new cases/year) neuro-oncology centre, between 2016-2021. Having previously been analysed locally by limited directed immuno-histochemical stains and referral for specific genetic tests, tissue is now referred for a range of second histopathological opinions and in depth molecular classification, via methylation array, panel sequencing, RNA fusion analysis, and whole genome sequencing. These are accessed through different evolving pathways and consent processes, including referral to other centres, national reference laboratories, clinical studies, and local genetics laboratories with links to national sequencing infrastructures. Different routes result in different reporting structures, timescales and with varying levels of interpretation, often without adequate access to clinical information and context. 21 patients were treated on five targeted agent clinical trials (Afatanib (n=6), Biomede (n=3), eSmart(n=1), PARC (n=7), Vinilo (n=5)), with one patient on both Afatanib and PARC trials. A further two patients visited other centres for trials. Eight patients received MAPK pathway inhibitors through compassionate access pathways, with benefit, including radiological response, in four. Cardiac toxicity was observed in three and retinal oedema in one. Two patients received immune checkpoint inhibition, with rapid fatal enlargement, either progression or pseudo-progression, in one case. These rapid changes in diagnostic and management options offer new opportunities for patients, but bring challenges to the delivery of neuro-oncology services, including the logistics of sample, report, clinical trial, compassionate access management and the increased multi-specialist support required for monitoring and management of toxicities. Integration of targeted agents into the appropriate part of a patient's treatment strategy requires skilled interpretation of the benefits compared to conventional therapies.

**OTHR-21. ETHICAL REFLECTIONS VIA THE DILEMMA METHOD IN A PEDIATRIC NEURO-ONCOLOGY DEPARTMENT**

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BACKGROUND: Professional care for children with a brain tumor can bring considerable ethical questions in clinical practice. These questions can be burdensome and cause distress among professionals, parents and patients. Awareness and skills to bring these aspects into a respectful discussion among colleagues can be meaningful and alleviate the distress. Our objective is to give overview of the ethical case deliberations which took place during a monthly multidisciplinary meeting on the pediatric neuro-oncology department. METHOD: To describe the type of ethical case deliberations as spontaneously proposed and selected by the team members for discussion. To identify main values in the care process for professionals via the dilemma method in monthly meetings led by a trained facilitator. RESULTS: The monthly meetings were visited regularly by 9-14 diverse professionals (median 10) of the team: nurses, oncologists, social worker, psychologist, educational specialist. The selected moral questions concerned children with a brain tumor between 4-13 year old (median 9) with following ten subjects: 3 not sharing the infaust prognosis with a child, 2 avoiding medical care in follow up /treatment, 2 cultural different approach for food and drink intake, 2 crossing professional boundaries and 1 time worries about emotional safety of a child. The main values that were recognized to play crucial role in the care process were honesty, respect, autonomy, quality of life, health, tolerance, courage and safety. The participants felt supported in their professional skills by sharing reflections on personal moral considerations and by openly discussing different views and experiences of other participants. CONCLUSION: The monthly ethical case discussions disclose high lights in the burden of professional care in pediatric neuro-oncology. These meetings about moral questions are supportive in the competence of the professionals to recognize and communicate about these important dilemmas.

**OTHR-22. MALIGNANT MESOTHELIOMA (MM) AS SECOND CANCER IN CHILDHOOD BRAIN TUMOR SURVIVORS: THE FIRST CHILD WITH NEUROFIBROMATOSIS TYPE 2 AND CONCURRENT MM**

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We report two cases of malignant mesothelioma (MM) in childhood brain tumor survivors. A 40-year-old man, who was treated at the age of ten with chemotherapy and craniospinal radiotherapy (up to 54.5 Gy) for a pineal secreting non-germinomatous germ cell tumor, had persistent fever, fatigue, and weight loss. A total body CT scan revealed several pulmonary and abdominal wall nodularities. The histological examination on a biopsy diagnosed a biphasic MM. The karyotype and array-CGH of peripheral blood were normal; a FISH of tumor cells showed a breakage of locus EWSR1 (22q12.2). In this case, environmental exposure was identified (asbestos in public water tanks). His MM followed an aggressive course and resulted in death after three months. A twelve-year-old boy affected by severe neurofibromatosis type 2 (NF2) already treated with several neurosurgical exeresis and chemotherapy lines (hydroxycarbamide, bevacizumab, sirolimus), developed multiple abdominal lesions, associated with pleural effusion and weight loss. The CT scan showed the thickening of the left pleura and multiple peritoneal nodules. The cytological examination on thoracentesis