(n=4) and 3 non-recurrent ACP were analysed using β-catenin, pERK1/2 immunostaining, DNA methylation array and RNA sequencing. Differential expression and methylation analyses confirmed differences between ACP and PCP, with over representation of WNT pathway genes in ACP and the MAPK pathway genes in PCP. All of the primary and all except for one of the relapsed ACP tumours showed a pERK1/2 expression. Differences in the immune environment were also identified between ACP and PCP, with higher levels of some inflammatory mediators and CD14+ cell signatures in PCP compared with ACP. Whilst differential methylation and expression analysis revealed relatively stable methylomes and transcriptomes between serial samples of cases, segmental chromosomal alterations were identified in recurrence samples from five ACP cases (5/11,45%). One relapsed case showed histological and molecular signs of malignant transformation, including high ki67 and deletion of *TP53*. Surprisingly, this malignant tumour showed nuclear beta-catenin in all neoplastic epithelial cells and absence of pERK1/2 staining, despite the primary tumour showing the typical beta-catenin and pERK1/2 expression patterns. These results suggest that the molecular landscape of craniopharyngioma remains stable between recurrences in most cases, but, there is evidence of molecular evolution in a subset of cases. Activation of the MAPK pathway in the vast majority of ACP tumours supports the clinical evaluation of MAPK pathway inhibitors in ACP patients.

RARE-09. TREATMENT OF CHILDHOOD-ONSET CRANIOPHARYNGIOMA PATIENTS USING PROTON BEAM THERAPY VERSUS PHOTON-BASED RADIATION THERAPY IN THE PROSPECTIVE KRANIOPHARYNGEOM 2007 TRIAL

Carsten Friedrich[1], Svenja Boekhoff[1], Panjarat Sowithayasakul[1,2], Maria Eveslage[3], Brigitte Bison[4], Beate Timmermann[5], Hermann L. Müller[1]; [1]Dep. of Pediatrics and Pediatric Hematology / Oncology, University Children's Hospital, Klinikum Oldenburg AöR, Carl von Ossietzky University, Oldenburg, Oldenburg, Germany. [2]Department of Pediatrics, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand. [3]Institute for Biostatistics and Clinical Research, University of Münster, Münster, Germany. [4]Department of Neuroradiology, University Hospital Augsburg, Augsburg, Germany. [5]Department of Particle Therapy, University Hospital Essen, West German Proton Therapy Centre Essen (WPE), West German Cancer Centre (WTZ) and German Cancer Consortium (DKTK), Germany, Essen, Germany

BACKGROUND: Proton beam therapy (PBT) compared to photon-based radiotherapy (XRT) offers the benefit to administer lower radiation doses to critical organs thereby possibly minimizing the risk of sequelae in patients with residual craniopharyngiomas (CP) after hypothalamus-sparing surgery. The validation in large CP patient cohorts is still pending. PATIENTS AND METHODS: Of 290 childhood-onset CP patients included 2007-2019 in the prospective multicenter trial KRANIOPHARYNGEOM 2007, 99 (34%) received external RT (65% PBT, 35% XRT). Outcome was compared between the different groups in terms of overall (OS) and event-free survival (EFS), quality of life (QoL using PEDQOL), functional capacity (FMH), and auxological data (BMI and height SDS) one, three and five years after irradiation/CP diagnosis. RESULTS: PBT became the predominant irradiation technique during the study period (used in 23% and 77% of all irradiated patients registered within the first and second half of the enrollment period, respectively). PBT as well as XRT were associated with high ($p<0.001$) EFS (PBT: 0.917 ± 0.040; XRT: 0.940 ± 0.041) compared to non-RT (EFS: 0.669 ± 0.044). OS was similar in all groups. No differences between PBT, XRT and non-RT CP patients concerning functional capacity and anthropometric parameters (height SDS, BMI SDS) have been obtained. Only in the PEDQOL domain "physical function", proxy-assessed QoL was lower one year after PBT when compared to XRT treated and non-irradiated CP patients. **CONCLUSION**: PBT is similar efficient in preventing relapses and recurrences in childhood-onset CP patients. During follow-up, no clinically relevant differences between PBT and XRT in terms of QoL, functional capacity and degree of obesity as a marker of hypothalamic syndrome were detectable. While PBT is increasingly applied, studies on larger CP cohorts with longer follow-up after RT are warranted to analyze, whether it can prevent sequelae such as hypothalamic syndrome and severe obesity compared to XRT.

RARE-10. NEUROCUTANEOUS MELANOCYTOSIS-ASSOCIATED HYDROCEPHALUS: THE MSK EXPERIENCE FROM 2001-2022

Scarlett Rodriguez[1], Ugur Sener[2], Kevin Elmore[3], Sofia Haque[1,4], Stephanie Suser[1], Jeffrey Greenfield[1,4], Maria Donzelli[1], Courtnee DePass[1], John Pugh[5], Joanne Porter[5], Nathan Meeker[6], Elizabeth Wells[7], Ashfaq Marghoob[1], Yasmin Khakoo[1,4]; [1]Memorial Sloan Kettering Cancer Center, New York, NY, USA. [2]Mayo Clinic, Rochester, MN, USA. [3]The Mount Sinai Hospital, New York, NY, USA. [4]New York-Presbyterian: Weill Cornell Medical Center, New York, NY, USA. [5]Albany Medical Center, Albany, NY, USA. [6]St. Luke's Children's Cancer Institute, Boise, Idaho, USA. [7]Children's National Hospital, Washington, DC, USA

OBJECTIVE: We hypothesize that patients with neurocutaneous melanocytosis-associated melanoma and ventriculoperitoneal shunts are at risk of developing intraperitoneal spread of melanoma. BACKGROUND: Neurocutaneous melanocytosis, a rare condition characterized by excessive proliferation and deposition of melanocytes in the leptomeninges and brain parenchyma, typically occurs in children with large congenital melanocytic nevi and multiple smaller congenital nevi. These patients are at heightened risk for developing NRAS+ melanomas in the central nervous system, which in turn may lead to symptomatic hydrocephalus requiring cerebrospinal fluid diversion for symptom relief. METHODS: Retrospective single-institution study of patients with histologically or radiographically confirmed NCM evaluated at Memorial Sloan Kettering Cancer Center (MSKCC) from 2001-2022. RESULTS: Of the 47 patients with a diagnosis of NCM, 44 patients had symptomatic neurological complications. Eleven patients developed hydrocephalus, 10 had CNS melanoma, and required ventriculoperitoneal shunt placement. Nine of the 10 patients ultimately died of their disease. Three patients were diagnosed with intraperitoneal melanoma, though data are unavailable for the remaining eight. CONCLUSIONS: All (n=11) patients with NCM-associated CNS melanoma required VP shunts for symptomatic relief. Ten of these patients died within 4.3 years of VP shunt placement, with a range of 1 month to 13.5 years prior to succumbing to their disease. While the intraperitoneal pathology remains unknown for 7 of the cases, 3 had confirmed intraperitoneal melanoma, suggesting that VP shunts provided the conduit to CNS melanoma seeding of the peritoneum. Obtaining baseline abdominal imaging studies prior to VP shunt placement may be helpful in the follow-up of these patients.

RARE-11. 60 YEARS SINGLE CENTRE EXPERIENCE OF CRANIOPHARYNGIOMA MANAGEMENT

Beryl Rodrigues[1], Jenny Adamski[1], Martin English[1], Helen Curry[2], Guirish Solanki[1], Andrew Peet[1,3], John Apps[1,3]; [1]Birmingham Women's and Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom. [2]West Midlands Regional Children's Tumour Registry, Birmingham, United Kingdom. [3]University of Birmingham, Birmingham, United Kingdom

Adamantinomatous craniopharyngiomas are challenging intracranial tumours associated with significant morbidity. Management includes surgery and radiotherapy, with a shift towards more conservative surgery in recent years, aimed at preserving hypothalamic function. The West Midlands Regional Children's Tumour Registry collects detailed clinical, pathological and follow up information on patients treated within the region from 1957. 52 cases (26 male, 26 female) of craniopharyngioma treated at Birmingham Children's Hospital 1957-2018, were identified, with further clinical details obtained from patient records, where available. Visual symptoms were the commonest presenting feature (63%), followed by headache (48%), vomiting (31%), neurological symptoms (31%) and features of endocrine disorders (21%) with a median symptom duration of 6 months (range <1-24). Initial management was with gross total resection (GTR) in 14 patients, subtotal resection in 22 patients and subtotal resection with adjuvant radiotherapy in seven patients. Two patients received radiotherapy without resection, and five patients underwent cystic drainage procedures alone. Two patients initially underwent shunt insertion alone, but received radiotherapy at progression. 30 (58%) patients underwent relapse/progression, with a median time to progression of 1.2 years (range 0.2-6.3). 15 had further surgery. Radiotherapy was used in 14/15 patients who had not previously received radiotherapy, with the other undergoing a GTR. To date 10 patients have died, nine from tumour related reasons and one from pulmonary embolism. Where data was available at follow up, all patients had at least one endocrinopathy, with 38/45 patients having diabetes insipidus. Hypothalamic obesity was identified in 14/36 (39%) patients with sufficient records, with this more common in those undergoing GTR (7/9 (78%)) compared to other surgical procedures (7/27)(26%)($p<0.05$). Three patients have developed neurovascular complications and three fatty liver disease. This experience is consistent with the literature and supports the increasing usage of hypothalamic sparing surgical management.

RARE-12. PINEOBLASTOMA OF CHILDREN AND YOUNG ADULTS IN A NATIONAL POPULATION: AN ANALYSIS OF THE HIT-MED STUDY COHORT

Mathias Yuan[1], Martin Mynarek[1], Tobias Goschzik[2], Elke Pfaff[3,4], Rolf Kortmann[5], Brigitte Bison[6], Monika Warmuth-Metz[6], Ulrich Schiller[7,8], Christian Hagel[9], Denise Obrecht[1], Martin Benesch[10], Stefan M. Pfister[11,3], Torsten Pietsch[2], Stefan Rutkowski[1]; [1]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [2]Department of Neuropathology, University of Bonn, Bonn, Germany. [3]Hopp Children's Cancer Center Heidelberg (KiTZ), Division of Pediatric Neurooncology, Heidelberg, Germany. [4]Pediatric Glioma Research Group (B [360]), German Cancer Research Center (DKFZ),, Heidelberg, Germany. [5]Department of Radiation Oncology, Leipzig, Germany. [6]Institute of Diagnostic and Interventional Neuroradiology, University Hospital Wuerzburg, Wuerzburg, Germany. [7]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Research Institute Children's Cancer Center Hamburg, Hamburg, Germany. [8]Institute of Neuropathology, University

Medical Center Hamburg-Eppendorf, Hamburg, Hamburg, Germany. [9]Institute of Neuropathology, University Medical Center, Hamburg-Eppendorf, Hamburg, Hamburg, Germany. [10]Department of Paediatrics and Adolescent Medicine, Medical University of Graz, Graz, Austria. [11]German Cancer Consortium (DKTK) and German Cancer Research Center (DKFZ), and Department of Pediatric Oncology, Hematology and Immunology, Heidelberg University Hospital, Heidelberg, Germany

BACKGROUND: Pineoblastoma is a malignant tumor of the pineal gland and accounts for <1% of all pediatric brain tumors. **PURPOSE/** METHODS: Patients <21 years (y) with pineoblastoma confirmed by central neuropathology review between 2001–2021 and included into the HIT2000 trial, HIT2000interim- or I-HIT-MED-registries were eligible. RESULTS: 88 patients were identified. Age at diagnosis was 0.01–20.71y (median 9.34y), median follow-up was 6.54y (IQR 1.78–12.41y) in 48 patients alive at last follow-up. 20 patients were <4y and received chemotherapy with intent to avoid radiotherapy. Of these, 7 patients were alive at last follow-up, two patients were radiotherapy-naïve and 5 patients had undergone CSI + boost (4 after incomplete response and one after progression). 5-y-PFS/OS in 68 patients >4y differed according to metastatic status (M0 (n=40) 72.7±8.3%/75.0±8.3%; M+ (n=28) 28.7±10.3%/40.8±10.9%, p=0.001/0.001). Therapy escalation in M0 patients by giving SKK chemotherapy before radiotherapy did not improve PFS/OS compared to upfront radiotherapy (5-y-PFS/OS 70.7±14.3%/70.0±14.5% vs 74.2±10.1%/78.9±9.4%, p=0.61/0.73). Applied CSI dosages were 24–50Gy (mean 35.6Gy) with no prognostic value of specific dosages being observed. Similarly, in M0 patients hyperfractionated radiotherapy (2x1.0Gy/d, total dose (TD) 36Gy, n=23) was not superior to conventional radiotherapy (1.6Gy/d, TD 35.2Gy, n=7). In all patients, favorable prognostic factors were age >4y (5-y-PFS/OS 54.1±7.0%/60.0±7.0% vs 30.0 ±10.2%/35.0±10.7%, p=0.012/0.053) and radiotherapy in primary therapy (5-y-PFS/OS 55.8±6.5%/61.4±6.4% vs 14.4±9.4%/21.4±11.0%, p<0.001/=0.003), whereas unfavorable prognosis was associated with metastatic disease (5-y-PFS/OS 33.6±9.0%/45.9±9.3% vs 58.8±7.6%/59.3±7.7%, p=0.028/0.086). **CONCLUSION:** Survival is poor in pineoblastoma patients <4y treated without radiotherapy. Unfavorable prognosis was associated with metastatic disease, especially in older children. Chemotherapy combined with CSI is effective for non-metastatic patients at age >4y. Further research will consider biological subgroups to enhance risk stratification and identify approaches for therapy improvements.

RARE-13. CLINICAL MANAGEMENT AND FUNCTIONAL AND SURVIVAL OUTCOMES IN PEDIATRIC CRANIOPHARYNGIOMA, A PATIENT AND FAMILY PERSPECTIVE

Emily Marshall[1], Sylvia Cheng[2], Julia Crowley[3], Shana McCormack[3], Brian Rood[4], Todd Hankinson[5], Michael DeCuypere[6], Sandy Lam[6], Stewart Goldman[7], Svenja Boekhoff[8], Hermann L Muller[8], Ryan Velasco[9], Phillip B Storm[3], Adam Resnick[9], Michael Prados[10], Sabine Mueller[10], Cassie Kline[3], Fatema Malbari[11]; [1]Sidney Kimmel Medical College, Philadelphia, Pennsylvania, USA. [2]BC Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada. [3]Children's Hospital of Philadelphia, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA. [4]Children's National Hospital, Washington DC, USA. [5]Children's Hospital Colorado, University of Colorado Medicine, Aurora, Colorado, USA. [6]Lurie Children's Hospital, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA. [7]Phoenix Children's Hospital, University of Arizona College of Medicine, Phoenix, Arizona, USA. [8]University Children's Hospital, Carl von Ossietzky University Oldenburg, Klinikum Oldenburg AöR, Oldenburg, Germany. [9]Center for Data-Driven Discovery in Biomedicine/Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA. [10]University of California San Francisco Benioff Children's Hospital, San Francisco, California, USA. [11]Texas Children's Hospital, Baylor College of Medicine, Houston, Texas, USA

Craniopharyngiomas are rare, histologically benign, sellar/parasellar tumors with significant tumor and therapy related morbidity and impairment in quality of life (QOL). We report survey results from patients/families affected by childhood-onset craniopharyngioma to identify opportunities for improvement in management. An anonymous REDCap survey was distributed via social media and clinic visits to patients/families of craniopharyngioma survivors. Survey questions investigated perspectives on clinical management and functional and survival outcomes at initial diagnosis and recurrence. A total of 159 patients/families completed the survey, 40% (n=64) reported craniopharyngioma recurrence. For primary craniopharyngioma, maximal safe resection was the most frequent treatment reported (n=84), followed by partial resection (n=40), radiation (n=8), biopsy (n=5), and chemotherapy (n=3). Most patients (n=120) decided on a treatment plan within one week, 63 (40%) decided in one day. For recurrent craniopharyngioma, maximal safe resection and radiation were the most frequent interventions (n=33 each), followed by partial resection (n=13), chemotherapy (n=4) and biopsy (n=2). Multiple treatment options and/or participation in a clinical trial were offered to similar numbers of patients across primary and recurrent diagnoses (~21% for each). Most recurrent craniopharyngioma patients decided on management within one week (n=43). Long term effects related to tumor and treatment were identified as the primary concern in all respondents. The most common deficits for all patients were neuro-endocrine followed by vision and neurocognition problems. Neuro-endocrine complications were self-reported as the biggest impact on QOL. Families reported that they would prefer treatment options with the potential for improved QOL, even if these options also carried an increased risk of recurrence. Craniopharyngioma continues to be predominantly treated with surgery and radiation initially and with recurrence. Survivors have multiple comorbidities, with an interest in targeted therapies that preserve QOL. Novel therapies to prevent co-morbidities and provide long term benefits are necessary and upcoming.

RARE-14. NEWBORN WITH HYPOTHALAMIC HAMARTOMA AND PALLISTER-HALL SYNDROME

Anna Meera Flaßkühler[1], Carsten Friedrich[1], Julia Beckhaus[1], Svenja Boekhoff[1], Kai Fiedler[2], Mechthild Schulze Becking[2], Marc-Philipp Hitz[3], Laura Gieldon[3], Stephanie Spranger[4], Brigitte Bison[5], Florian Hoppe[6], Hermann L. Müller[1]; [1]Dept. of Pediatrics and Pediatric Hematalogy / Oncology, University Children's Hospital, Klinikum Oldenburg AöR, Carl von Ossietzky University, Oldenburg, Oldenburg, Germany. [2]Dept. of Pediatric and Neonatal Intensive Care Unit, University Children's Hospital, Klinikum Oldenburg AöR, Carl von Ossietzky University, Oldenburg, Oldenburg, Germany. [3]Insitute for Medical Genetics, Carl von Ossietzky University, Oldenburg, Oldenburg, Germany. [4]Practice of Human Genetics, Bremen, Germany. [5]Dept. of Neuroradiology, University Hospital of Augsburg, Augsburg, Germany. [6]Dept. of Otorhinolaryngology-Head and Neck Surgery, Klinikum Oldenburg AöR, Carl von Ossietzky University, Oldenburg, Oldenburg, Germany

A female full-term newborn of 41 + 2 weeks gestational age with a respiratory adaptation disorder and hypercapnia was transferred from an external maternity clinic to our pediatric intensive care unit. The child is the second child of healthy, non-consanguineous parents. Multiple dysmorphias were noticed at arrival. We identified a choanal atresia/stenosis on both sides in the respiratory tract, a high palate, a submucous cleft palate, a bifid uvula, a laryngeal cleft and a bronchus suis. The child required intubation and ventilation. In addition, we recognized brachydactyly of the hands and feet. The phalanges were not visibly separable. There was nail hypoplasia and rocker bottom feet on both sides. Furthermore, we saw an anal atresia. In routine laboratory work-up, a hypoglycemia and not measurable low TSH serum concentration was noticed. Extended endocrinological laboratory diagnostics revealed a complete pituitary insufficiency. On cranial MRI, a large, iso- to slightly hyperintense space-occupying mass (3.8x3.7x2.5 cm^3), originating from the hypothalamus was observed. The brainstem was displaced posteriorly by the mass. The imaging is consistent with a hypothalamic hamartoma. With regard to the present findings, we assumed an underlying genetic cause of the congenital malformations. As a clinical diagnosis, a Pallister-Hall syndrome was suspected. As described in our case, we saw the characteristic features: dysmorphia of the hands and feet, upper respiratory tract, anal atresia, and hypothalamic hamartomas. The Pallister-Hall syndrome is caused by mutations in the GLI3 gene on the 7p13 chromosome. It is inherited in an autosomal dominant manner and its prevalence is unknown. In our patient, a heterozygous, probably pathogenic variant in the GLI3-Gene was proven by Next Generation Sequencing (NGS).

RARE-15. ASTROBLASTOMA, *MN1* ALTERED COMPRISES TWO MOLECULARLY AND CLINICALLY DISTINCT SUBGROUPS DEFINED BY THE FUSION PARTNERS *BEND2* AND *CXXC5*

Felix Schmitt-Hoffner[1], Johannes Gojo[2,1], Monika Mauermann[1], Katja von Hoff[3], Martin Sill[1], Damian Stichel[4], David Capper[5,6], Arnault Tauziede-Espariat[7], Pascale Varlet[7], Kenneth Aldape[8], Zied Abdullaev[8], Andrew M. Donson[9], Ulrich Schüller[10], Matija Snuderl[11], Sebastian Brandner[12], Maria Łastowska[13], Joanna Trubicka[13], Evelina Miele[14], Jasper van der Lugt[15], Jens Bunt[15], Christof Kramm[16], Michal Zapotocky[17], Felix Sahm[1,18], Andrey Korshunov[4,19], Natalie Jäger[1], Stefan M. Pfister[1,20], Marcel Kool[1,15]; [1]Hopp-Children's Cancer Center Heidelberg (KiTZ), Heidelberg, Germany. [2]Medical University of Vienna, Vienna, Austria. [3]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany. [4]Heidelberg University Hospital, Heidelberg, Germany. [5]Department of Neuropathology, Charité Universitätsmedizin Berlin, Berlin, Germany. [6]German Cancer Consortium (DKTK), Partner Site Berlin, Heidelberg, Germany. [7]Department of Neuropathology, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, Paris, France. [8]Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. [9]Morgan Adams Foundation Pediatric Brain Tumor Research Program, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA. [10]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [11]Department of Pathology, New York University School of Medicine, New York, NY, USA. [12]Department of Neurodegeneration, Institute of Neurology, University College London, London, United Kingdom. [13]Department of Pathomorphology, The Children's Memorial Health Institute, Warsaw, Poland. [14]Department of Oncology, Hematology, Cell Therapy, Gene Therapy and Haemopoietic Transplant, Bambino Gesù Children's Hospital,