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,

IRCCS, Rome, Italy. [15]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands. [16]Division of Pediatric Hematology and Oncology, University Medical Center Goettingen, Goettingen, Germany. [17]Prague Brain Tumor Research Group, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic. [18]Department of Neuropathology, Heidelberg University Hospital, Heidelberg, Germany. [19]Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany. [20]Department of Pediatric Hematology and Oncology, Heidelberg University Hospital, Heidelberg, Germany

In the recent 5th edition of the WHO classification of CNS tumors, 'Astroblastoma, *MN1* altered' is recognized a distinct brain tumor type, occurring in children and young adults. Due to its rarity and novelty, little is known about clinical and molecular traits. Therefore, we initiated an international effort and collected tissue samples, clinical and molecular data from 176 patients with Astroblastoma, *MN1* altered, identified by their distinct DNA methylation profiles. DNA methylation-based *t*-SNE clustering analyses revealed that Astroblastoma, *MN1* altered tumors form one distinct main cluster (n=158) showing *MN1:BEND2* and single cases with *EWSR1:BEND2* fusions and a further adjacent, but distinct smaller cluster (n=18) mostly defined by *MN1:CXXC5* fusions. Both fusion partner-defined groups show a median age of 12 years but distinct copy-number aberrations, characteristically a gain of chromosome 5 in one third of the *CXXC5*-fused group and a loss of chromosome 16q in one third of *BEND2*-fused cases. As previously reported, a vast majority of Astroblastoma, *MN1* altered patients are female, which we confirm for the *BEND2*-fused group (85%). The *CXXC5*-fused group, however, shows 75% male patients. Interestingly, 9/10 tumors of the few male patients observed in the *BEND2*-fused group were all located infratentorially or in the spinal cord, whereas almost all female cases show a supratentorial location (85/87). Histologically, the *BEND2*-fused group was primarily reported as Astroblastoma (39%), whereas in the *CXXC5*-fused cases, 31% CNS-PNET and only 8% Astroblastoma histologies were originally assigned. Preliminary clinical analyses showed that the *BEND2*-fused group has a relatively good 5/10-year OS of 97%/89%, but a less favorable 5/10-year PFS of 48%/35%, in line with previous studies. Patients showing CXXC5-fused tumors (n=8) indicated 5/10-year OS and PFS rates of 83%/83% and 60%/60%, respectively. Additional survival and molecular analyses are being conducted to further characterize Astroblastoma, *MN1* altered tumors and its molecular subgroups.

RARE-16. DIFFERENTIAL EXPRESSION OF MIRNAS IN ADAMANTINOMATOUS CRANIOPHARYNNGIOMA REVEALS DYSREGULATION OF PATHOGENIC PATHWAYS

John Apps; University of Birmingham, Birmingham, United Kingdom. University College London, London, United Kingdom

MicroRNAs (miRNAs) are small non-coding RNAs that regulate the expression of target mRNAs and can control whole gene networks. ACPs are benign pituitary tumours that can result in significant morbidity and premature mortality. ACPs harbour mutations in CTNNB1 and are driven by the activation of the WNT/beta-catenin pathway. We sought to explore the expression of miRNAS in adamantinomatous craniopharyngioma (ACP) in a cohort of samples previously subjected to RNA-Seq analysis (Apps et al, Acta Neuropathologica, 2018, May;135(5):757-777). Total RNA ACP samples (n=18), non-functioning pituitary adenomas (n=3) and normal foetal pituitaries (n=3) underwent miRNA sequencing using the Qiagen miRNA library prep kit on a NextSeq 500 to a depth of 16 million reads. Differential expression was performed using DESeq2 and functional analysis with mirPath v.3. Expression of miRNAs was correlated with previously published mRNA expression We found that 210 miRNA were upregulated and 275 down regulated in ACP compared with controls (adjusted p-value <0.1). MIR-205-5p was the most upregulated miRNA (619 fold) and its expression correlated with genes expressed within the tumour epithelium (e.g. TP63). miR-375 an inhibitor of the WNT pathway was the most down regulated miRNA (361 fold). KEGG Pathway analysis identified Glycosphingolipid synthesis as the most enriched pathway targeted by upregulated miRNAs. Pathways that were enriched by down regulated miRNAs included: ECM-receptor interaction, fatty acid biosynthesis, Hippo, TGF-beta, WNT, and ErbB pathways. Down regulation of miR-132 has previously been suggested as a marker of aggressiveness in ACP, and was 16 fold down regulated (adjusted p-value<0.001) in this cohort and expression was inversely correlated with genes relating to epithelial development. This data confirms previous studies indicating that miRNA expression is altered in ACP. In silico analysis suggest that the dysregulation of miRNA affects the expression of genes involved in pathogenic pathways in ACP.

RARE-17. MULTI-INSTITUTIONAL CRANIOPHARYNGIOMA COHORT HIGHLIGHTS NEED FOR MORE COMPREHENSIVE DATA COLLECTION ON COMORBIDITIES AND QUALITY OF LIFE

Emily Marshall[1], Julia Crowley[2], Shana McCormack[2], Brian Rood[3], Todd Hankinson[4], Sylvia Cheng[5], Michael DeCuypere[6], Sandi Lam[6], Stewart Goldman[7], Lance Ballester[8], Walter Faig[8], Ryan Velasco[2], Kamnaa Arya[2], Phillip Jay B Storm, Jr.[2], Adam Resnick[2], Michael Prados[9], Sabine Mueller[9], Fatema Malbari[10], Cassie Kline[2]; [1]Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, USA. [2]Children's Hospital of Philadelphia, Philadelphia, PA, USA. [3]Children's National Hospital, Washington, DC, USA. [4]Children's Hospital Colorado, Aurora, CO, USA. [5]BC Children's Hospital, Vancouver, BC, Canada. [6]Lurie Children's Hospital of Chicago, Chicago, IL, USA. [7]Phoenix Children's Hospital, Phoenix, AZ, USA. [8]Westat, Rockville, MD, USA. [9]UCSF Benioff Children's Hospital, San Francisco, CA, USA. [10]Texas Children's Hospital, Houston, TX, USA

BACKGROUND: Pediatric craniopharyngioma is associated with long-term survival, but tumor- and therapy-related complications often negatively impact quality of life (QoL). Standard treatments include resection and radiation, but institutional practices vary and recurrence rates remain high. In this review, we utilized a cohort from the Children's Brain Tumor Network (CBTN) to evaluate outcomes for craniopharyngioma. METHODS: CBTN provides clinical and genomic data for pediatric patients diagnosed with primary central nervous system tumors across 25+ institutions. We collected data for 124 patients, ages 0-21, diagnosed with craniopharyngioma between 2012-2020. Variables collected included treatment, recurrence/progression, and comorbidities. RESULTS: Excluding patients without confirmed pathologic diagnosis (n=10) or follow-up data (n=39), 75 patients remained. For initial treatment, most (n=46, 61%) received surgery alone (9 partial, 33 near-total resection). Twenty-six (35%) underwent both surgery and radiation, with 9 receiving both therapies upfront and 17 receiving radiation at progression/recurrence. Four (5%) patients received chemotherapy. Over half of the cohort (n=39, 52%) had at least one progression/recurrence, and four died (5%). Significantly higher rates of progression/recurrence (84% vs. 32%, p=4.0e-5) were identified in patients that had surgery and radiation, compared to surgery alone. Time to recurrence, progression, or death was shorter for the surgery and radiation group (HR=4.1, p<1.0e-4), and for those that underwent partial versus near-total resection (HR=2.7, p=0.1.2e-2). Comorbidities were likely underreported, based on low rates of visual (32%), neuroendocrine (27%), and neurologic (28%) deficits at diagnosis, and 29 patients (39%) with unspecified medical history. CONCLUSIONS: CBTN provides a robust repository of information on treatment and survival of craniopharyngioma patients. However, we found a paucity of data on associated comorbidities and QoL outcomes. We advocate that future datasets and clinical trials routinely collect functional outcomes alongside therapy and survival data, particularly in craniopharyngioma where long-term survival is balanced with future QoL.

RARE-18. PEDIATRIC CRANIOPHARYNGIOMA; SINGLE CENTER EXPERIENCE IN 246 CASES WITH DIFFERENT MANAGEMENT MODALITIES

Mohamed El Beltagy, Abdelrahman Enayet, Rana Sameh; Children's Cancer Hospital, Egypt, Cairo, Egypt

PURPOSE: To report our experience with different craniopharyngioma management strategies done for 246 patients in a single institution during a period of 14 years. METHODS: The medical records of all children with the diagnosis of craniopharyngioma treated at Children's Cancer Hospital Egypt (CCHE-57357) during the period from July 2007 to December 2021 were retrospectively reviewed. RESULTS : our registry included 246 pediatric craniopharyngiomawith median age of 7.4 years old. The main strategies of management after initial surgery were follow up, radiotherapy or administration of intracystic interferone post ommaya insertion. The number of cases in each group were 92, 147,and three respectively. Three patients were not operated upon because of heavily calcified lesions, two of them received radiotherapy while the third was kept under follow up. Overall gross or near total total excision was achieved in 31.2 % , subtotal resection was the case in 42.1% while Ommaya insertion and biopsy was done in 21.1 % of cases. Total number of patients received radiotherapy initially or on progression was 195 patients(78.9%). The five-year overall survival was 88% (95% CI 82.9 – 93.1) while 5- year progression free survival (PFS) was 49.2% (95% CI 41.2—57.2). The five-year PFS rates for patients in the follow up group versus radiotherapy group were 25.2% and 68.7% respectively (P< 0.0001). Beta catenin was positive in 76.4% of cases that were available for testing (123/161). CONCLUSION: management of craniopharyngioma should be individualized with the main objective is the quality of life. Conservative surgery which entails gross total safe resection whenever possible or lesser extent of resection followed by radiotherapy is the main strategy followed in our institution.

RARE-19. MOLECULAR CHARACTERIZATION AND TREATMENT RESPONSE OF METASTATIC DIA/DIG

James Petropoulos, Melanie Finkbeiner, Zarina Assis, Clare Gallagher, Walter Hader, Jennifer Chan, Douglas Strother, Lucie Lafay-Cousin; Alberta Children's Hospital, Calgary, AB, Canada

INTRODUCTION: Desmoplastic infantile astrocytoma (DIA) and desmoplastic infantile ganglioglioma (DIG) are glioneuronal tumors of early childhood. Surgical resection is usually sufficient to cure these benign