IRCCS, Rome, Italy. 13Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands. 14Division of Pediatric Hematology and Oncology, University Medical Center Goettingen, Goettingen, Germany. 15Prague Brain Tumor Group, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic. 16Department of Neuropathology, Heidelberg University Hospital, Heidelberg, Germany. 17Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany. 18Department 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 z-SNE clustering analyses revealed that Astroblastoma, MN1 altered tumors form one distinct main cluster (n=138) showing MN1:BEND2 and single cases with EWSR1:BEND2 fusions and a further adjacent, but distinct smaller cluster (n=18) mostly defined by MN1:CCX5:3 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 CCX5-fused group and a loss of chromosome 16 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 CCX5-fused group, however, shows 75% male patients. Interestingly, 910 tumors of the few male patients occurred in in one third of BEND2-fused cases with a gain in the spinal cord, whereas almost all female cases show a supratentorial location (85%). Histologically, the BEND2-fused group was primarily reported as Astroblastoma (39%), whereas in the CCX5-fused cases, 31% CNS-PNET and 1% glioblastoma. Genetic and 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 CCX5-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 CRANIOPHARYNGIOMA REVEALS DYSREGULATION OF PATHOGENIC PATHWAYS
John Apps1, 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 brain tumors that can result in significant morbidity and premature mortality. ACP’s harbors 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 craniopharyngiomas (ACP) in a cohort of samples previously identified in our recent RNA-Seq analyses (Apps et al, Acta Neuropathologica, 2018, 135(1):577-777). Total RNA ACP samples (n=18), non-functioning pituitary adenomas (n=3) and normal foetal pituitaries (n=3) underwent RNA isolation and 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%.

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 (CCHIE-57357) during the period from July 2007 to December 2021 were retrospectively reviewed. RESULTS: CBTN: 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 radiation 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/reurrence, and four died (5%). Significantly higher rates of progression/recurrence (84% vs. 32%, P=0.049) were seen in surgery and radiation group (HR:3.5, P=0.04). Conclusions: Our study shows that children with craniopharyngioma who undergo surgery and radiation therapy have higher rates of progression and recurrence compared to the surgery alone group (HR:4.1, P=0.004), and for those that underwent partial versus near-total resection (HR:2.7, P=0.02). 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-19. MOLECULAR CHARACTERIZATION AND TREATMENT RESPONSE OF METASTATIC DIA/DIG
James Petropoulos, Melanie Finkbeiner, Zarina Assis, Clare Gallagher, Walter Hader, Jennifer Chan, Douglas Stromher, Luce 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
tumors. The presence of metastatic seeding is rare and has been reported as an adverse prognostic factor. We present 2 cases of young children with recurrent metastatic DIA/DIG to describe their presentation, therapeutic management, and outcome and to highlight the importance of molecular characterization of these rare tumors to guide adjuvant therapy. CASES DESCRIPTION: The first patient developed metastatic recurrence after initial gross total resection (GTR) of a localized DIA. The disseminated relapse was treated with monthly carboplatin and vincristine (CBV) and was resistant. The second patient had complete response achieved after 15 cycles and the patient has remained in continuous complete remission for 5 years. Post hoc molecular analysis of the tumor revealed a BRAF-V600E mutation. The second patient presented with a disseminated intraventricular recurrence following an incomplete resection in a DIA associated with a suspectedNOTCH2 fusion. The patient received 2 cycles of CBV/C Rituximab with minimal response and was then switched to Larotrectinib leading to a very good partial response (VGPR) 3 months into therapy and has remained on treatment since then with significant clinical improvement. DISCUSSION/CONCLUSION: In our 2 cases of NOTCH-driven CP tumor recurrence, we observed tumor cells remain mono-ciliated and responsive to conventional chemotherapy in the first one and to VGPR with NTRK inhibitor in the second patient. Early molecular characterization of these benign tumors is critical in case of incomplete resection or metastatic seeding. Response with NTRK inhibitor appears rapid and significant but the total duration of treatment and sustainability of response after discontinuation remain unknown.

RARE-20. RETROSPECTIVE ANALYSIS OF 9 PINEOBLASTOMA
Kenu Ai, Juan Li, Mingyao Lai, Linbo Cai; Guangdong Sanjiu Brain Hospital, Guangzhou, Guangdong, China

BACKGROUND: Pineoblastomas (Pb)are rare, supratentorial, primitive neuroectodermal tumors. Little is known with the clinical features and outcomes of Pb. METHODS: Pb were retrieved whole-genome sequencing (WGS) and RNA-seq analysis. GBM with Pb were treated in Guangdong Sanjiu Brain Hospital between December 2006 to May 2020. RESULTS: A total of 9 patients (7 males and 2 females) with Pb were treated in our hospital with a median age of 9 years (range: 4-19 years). Total or partial resection was achieved in 3 patients (33%), partial resection in 4 (44.4%), and biopsy in 2 (22.2%). There were 4 patients have spinal cord metastasis at diagnosis. Five patients received craniospinal irradiation (CSI), with concurrent or adjuvant chemotherapy. Median total dose of CSI was 34.80±2.683Gy, and the average dose to local tumor bed was 56.08±6.41Gy. Two patients younger than 3 years old only received chemotherapy, while 1 patient did not receive any postoperative treatment, and 1 patient was unknown. The median follow-up time is 17 months(range:3-39 months). At the last follow up, 5 patients were died, 3 patients were survived, and 1 was lost to follow-up. The median OS was 31 months (95% CI 1.782-60.281). Disease progression occurred in 3 patients during the follow-up period, and the median PFS was 19 months. CONCLUSION: Pineoblastoma is a rare central nervous system malignancy with a tendency for disseminated disease. Comprehensive therapies such as surgical resection, radiation and chemotherapy are effective therapies for Pb.}

RARE-21 SOX2 PLAYS AN IMPORTANT ROLE IN CHOROID PLEXUS TUMOR DEVELOPMENT
Luka Faltings, Tamanna Sarowar, James Vogra, Navleen Singh, Brygdonia Kau, Hanatan Zhao; New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, USA

Choroid plexus (CP) tumors are rare primary brain neoplasms found most commonly in children and are thought to arise from CP epithelial cells. Sox2 is a transcription factor that not only plays a role in the development in the ventricular zone, CP, and roof plate, but also contributes to cancer stemness, tumorigenesis, and drug resistance. Gene expression studies demonstrate aberrant Sox2 expression in human CP tumors, suggesting a role in tumor development. A subset of CP tumors exhibit an abnormal NOTCH pathway activity. Using animal models, we previously showed that sustained NOTCH activity leads to CP tumors. Immunofluorescence, RT-qPCR, and RNA-seq analysis have revealed increased Sox2 expression in NOTCH-driven CP tumors with concurrent or adjuvant chemotherapy. To investigate the role of Sox2 in CP tumors, we eliminated Sox2 expression in NOTCH-driven CP tumors. Loss of Sox2 almost completely blocked NOTCH-driven CP tumor growth in these mice, supporting a role for Sox2 in these tumors. Ciliation regulation is one proposed functional pathway for tumorigenic mechanisms that advance our understanding of ACP biology.

RARE-22 CHARACTERIZING THE LANDSCAPE OF STRUCTURAL VARIANTS IN ADAMANTINOMATOUS CRANIOPHARYNGIOMA
Danny Joman, Prasuda Khadka, Dana Novikov;
Alexandra L. Condurache, Jessica W. Issacson, Frank Dubose, Shu Zhang, Kevin Zhou, Rose Goldel, Cecilia Sousa, Jane Vogelzang, Eric Princi, Sophie Lu, Veronika Silvova, Georg W. Otto, Sergi Castellano Herreraz, David Ashley, Aaron A. Cohen-Gadol, Eric Thompson, Rameen Beroukhim, John Apps, Juan Pedro Martinez-Barbera, Todd Heddle; A. Dana-Farber Cancer Institute, Boston, MA, USA. 2Children’s Hospital of Colorado School of Medicine, Aurora, CO, USA. 3Morgan Adams Foundation for Pediatric Brain Tumor Research Program, University of Colorado School of Medicine, Aurora, CO, USA. 4Milken Institute of Public Health, George Washington University, Washington, DC, USA. 5Indiana University Health, Indianapolis, IN, USA. 6University College London, London, England, United Kingdom. 7Department of Neurosurgery, Duke University, Durham, NC, USA. 8Department of Neurosurgery, Indiana University, Indianapolis, IN, USA. 9Brigham and Women’s Hospital, Boston, MA, USA. 10University of Birmingham, Birmingham, England, United Kingdom.

INTRODUCTION: Adamantinomatous craniopharyngiomas (ACP) are rare brain tumors that primarily occur in children and impact long-term morbidity and mortality. The molecular driver mutational signature in ACPs is unknown. Here, we performed whole-genome sequencing (WGS) and RNA-seq analysis of 41 ACP samples. MATCHED normal samples were also characterized by WGS. Mutec2 was used to detect single nucleotide variants (SNVs) and indels, and copy number data was generated using the GATK pipeline. SvaBA was used to perform SV analyses and to identify significantly recurrent breakpoints and juxtapositions. DESeq2 was used to perform differential gene expression analysis based on clinical and molecular annotation data. RESULTS: 29/41 (70%) of the ACP samples harbored missense mutations in CTNNB1, all of which have previously been identified in GBM. A total of 123 differentially expressed genes with q-value < 0.05. CONCLUSION: This study identifies activating mutations in exon 3 of CTNNB1 in a large cohort of ACP samples. We also integrate SV and transcriptomic data to comprehensively investigate ACP tumor genomes and identify putative novel tumorigenic mechanisms that advance our understanding of ACP biology.

RARE-23. PRESERVATION OF ENDOCARDIAL FUNCTION AFTER OMMAYA RESERVOIR INSERTION IN CHILDREN WITH CYSTIC CRANIOPHARYNGIOMA
Laura-Nanna Lokhamp, Abhaya V Kulkarni, James Drake, James T Rutka, Jill Hamilton, Ute K Bartels; The Hospital for Sick Children, Toronto, Ontario, Canada

INTRODUCTION: Children with craniopharyngiomas (CP) can be subjected to significant morbidity caused by radical surgery and/or radiation with deleterious long-term consequences. Ommaya reservoir insertion (ORI) into cystic CP represents a minimally invasive procedure allowing immediate decompression and aims to avoid additional injuries. The purpose of this study was to determine the relevance of upfront ORI (+/- intracystic treatment) for preservation of endocardial function. METHODS: We performed a retrospective chart review of children with CP treated at the Hospital for Sick Children between 01/01/2000 and 15/01/2020 for review of endocrinological outcome after ORI. Endocardial function was reviewed at the time of initial surgery and throughout the course of follow-up. Event-free survival (EFS) was defined as the time to further surgical resection or irradiation. RESULTS: Seventy-nine patients were identified with a median age of 8.3 (range 2.1-18.0) years, 31 were males. Sixty-six patients underwent surgical treatment, including 41 ORI. ORI was performed as upfront treatment in 32 patients, 33 patients underwent partial or total resection and 1 patient did not receive any postoperative treatment. Forty-five of 79 patients had sufficient endocardial follow-up data. Endocardial function remained stable after ORI with an EFS of 27.64 ± (5.22) months. Surgical resection was associated with worsened endocardial function postoperatively with an EFS of 5.48 ± (1.74) months (p<0.001). CONCLUSIONS: Upfront ORI (+/- intracystic treat-