dren. In the last few years, tumor classification through DNA methylation profiling has been demonstrated to be a powerful diagnostic tool which could be especially informative in this setting. METHODS: We reviewed original diagnosis and molecular profile of childhood CNS embryonal tumors other than medulloblastoma or AT/RT from a retrospective single-center cohort. Sixteen FFPE tissue samples from 14 unique patients (diagnosed from 1996 to 2017) were analyzed using DNA methylation arrays and matched with the Heidelberg classifier. Then, cohort characteristics and outcome were re-evaluated according to the results of the array. RESULTS: Median age at diagnosis was 2.7 years; there was no statistically significant difference between ETMRs and CNS embryonal tumors, NOS. Male to female ratio was 4:3. Median OS was 17,5 months (IQR 10.2-103.3 months) and ETMRs presented the worst outcome. Methylation profiling matched with an adequate score in 50% of samples (8/16). DNA methylation profile was consistent with ETMR in two samples but only one showed amplification of C19MC. Seven CNS embryonal tumors, NOS were properly reclassified as supratentorial ependymoma and diffuse pediatric-type HGG (4 and 1) or better defined as CNS neuroblastoma, FOXR2-altered (2). Methylation profiling added a unique diagnostic contribution in 64.3% of all cases (9/14). After the integration of methylation array results, survival markedly differed according to the novel integrated diagnoses; supratentorial ependymomas presented the longest median OS while no patients refined as CNS neuroblastoma or HGG survived. CONCLUSIONS: Our study confirmed that DNA methylation profiling provides relevant information for the classification of rare neoplasms like CNS embryonal tumors. Especially for selected cases with ambiguous histology, implementation of this tool should be considered to improve diagnostic precision and tailor patients' management.

ETMR-08. TREATMENT STRATEGY FOR PINEOBLASTOMA IN INFANT

Mario Suzuki[1], Yuzaburo Shimizu[1], Osamu Akiyama[1], Junya Fujimura[2], Akihide Kondo[1]; [1]Department of Neurosurgery, Juntendo University Faculty of Medicine, Tokyo, Japan. [2]Department of Pediatrics and adolescent Medicine, Juntendo University Faculty of Medicine, Tokyo, Japan

Pineoblastoma is a rare malignant brain tumor that occurs in infancy and young adulthood. Although its prognosis has improved in recent years, it remains one of the difficult tumor types to treat. We will retrospectively review the treatment of pineoblastoma at our hospital and propose the possibility of a new treatment for this tumor type. Three cases were studied. All of them presented at less than three years of age and were treated for hydrocephalus simultaneously as the biopsy. Chemotherapy was administered after a possible resection, and local radiotherapy was administered at the age of 3 years. Overall survival ranged from 7 to 91 months, with one case of long-term survival. To date, the prognostic factors for pineoblastoma are the age of onset and the presence of radiation therapy. This is interpreted to mean that the prognosis is worse in infants and young children who cannot be immediately treated with radiation therapy, indicating that radiation therapy is essential for treating this tumor type. On the other hand, radiation therapy for infants can significantly interfere with the development of the central nervous system, and there is much controversy about its potential compatibility with tumor control. We have identified a favorable prognosis group based on the molecular biological background of this tumor type. We propose that early radiotherapy may improve the prognosis.

ETMR-09. *IN VITRO* MODELLING OF EMBRYONAL TUMORS WITH MULTILAYERED ROSETTES (ETMR) AND OTHER NOVEL BRAIN TUMOR TYPES.

Jens Bunt[1], Mieke Roosen[1], Phylicia Stathi[1], Panagiotis Polychronopoulos[1], Zelda Odé[1], Joris Maas[1], Marcel Kool[1,2]; [1]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands. [2]Hopp Children's Cancer Center (KiTZ), Heidelberg, Netherlands

Over the last decade, molecular characterization has resulted in many tumors previously classified as central nervous system primitive neuroectodermal tumors (CNS-PNETs) now being classified into their own distinct tumor types. These novel types are often characterized by very specific genomic aberrations. For instance, embryonal tumors with multilayered rosettes (ETMR) harbor amplifications of miRNA cluster *C19MC* or complex *DICER1* mutations, while in CNS neuroblastoma with *FOXR2* activation structural aberrations result in aberrant *FOXR2* expression. Despite the presence of distinct oncodrivers, our understanding of these tumors is still limited. To elucidate tumor biology and to discover tumor specific treatments, we need to uncover how these oncodrivers contribute to tumorigenesis. However, a bottleneck in basic and translational research of these novel tumor types, is the lack of representative preclinical models, especially in vitro. To overcome this hurdle, we aim to mimic tumor development in genetically modified brain organoids. Human brain organoids derived from pluripotent stem cells are generated to represent either the developing forebrain or cerebellum. To mimic oncodriving events, DNA plasmids are introduced via electroporation into the proposed cell-of-origin populations to knockout tumor suppressor genes or overexpress oncogenes. By detecting fluorescent proteins encoded by the plasmids, electroporated cells are followed over time. Based on our preliminary data, for instance, overexpression of *C19MC* results in ectopic expansion of the electroporated cells. Ongoing histological and molecular characterizations, including (single cell) transcriptomic and epigenomic analyses, will reveal to which extend these organoid models resemble the specific human tumor types. Although further validation is required, these organoid models provide a novel avenue to study especially brain tumor types with distinct oncodriving events for which patient-derived models have not yet been established. They also allow for in-depth analyses of the potential cells of origin and the contribution of different mutations to tumor biology.

ETMR-10. RETROSPECTIVE MOLECULAR RE-EVALUATION OF CNS PNETS; A POPULATION-BASED STUDY

Elizabeth Schepke[1,2], Maja Löfgren[2], Torsten Pietsch[3], Teresia Kling[2], Claes Nordborg[4], Thomas Olsson Bontell[4], Stefan Holm[5], Anders Öberg[6], Per Nyman[7], Marie Eliasson-Hofvander[8], Magnus Sabel[1,9], Birgitta Lannering[9], Helena Carén[2]; [11]Childhood Cancer Centre, Queen Silvia Children´s Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden. [22]Sahlgrenska Center for Cancer Research, Department of Laboratory Medicine, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [3]Department of Neuropathology, DGNN Brain Tumor Reference Centre, University of Bonn Medical Centre, Venusberg-Campus[1], Bonn, Germany. [4]Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [5]Department of Pediatrics, Karolinska University Hospital, Stockholm, Sweden. [6]Department of Woman's and Children's Health, Uppsala University, Uppsala, Sweden. [7]Department of Pediatrics, Linköping University, Linköping, Sweden. [8]Department of Pediatric Oncology and Hematology, Lund University, Lund, Sweden. [9]Department of Clinical Science, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

BACKGROUND: The heterogeneous group of tumors, primitive neuro-ectodermal tumors of the central nervous system (CNS-PNETs), is a group of rare childhood embryonal tumors associated with a poor prognosis. In recent years, molecular analyzes have shown that CNS-PNETs consist of high-grade gliomas (HGG), ependymomas, different embryonal entities like atypical teratoid /rhabdoid tumors (AT/RT), CNS neuroblastoma FOXR2 and embryonal tumor with multi-layered rosettes (ETMR). Each of these tumor types is unusual and long-term clinical follow-up data are sparse. METHODS: We retrospectively re-evaluated all children (0-18 years old) diagnosed with a CNS-PNET in Sweden during 1984-2015. In total, 88 supratentorial CNS-PNETs were identified in the Swedish Childhood Cancer Registry and from these formalin-fixed paraffin-embedded tumor material was available for 69 patients. All tumors were reviewed histopathologically by an experienced neuropathologist and were analyzed using genome-wide DNA methylation profiling and classified by the MNP brain tumor classifier. RESULTS: The largest entities, after re-evaluation, were HGG (30%), CNS NB-FOXR2 (12%), AT/RT (10%) and ETMR (8%). Some tumors were difficult to classify and will be further evaluated molecularly. Some examples: Best treatment results were seen for patients with CNS-NB FOXR2 (5-year PFS: 100%) where all patients had received craniospinal radiotherapy (CSI). Patients with ETMR were all very young and survival data show early progression and poor survival (5-year OS 34%). CONCLUSIONS: Although the patient material is relatively small, it is population-based with long follow-up times. Our findings are in line with other studies and shows that CSI is important for cure for CNS-NB FOXR2 and that intensive multi-modal therapies needs to be evaluated in up-front studies for these rare embryonal tumors.

ETMR-11. TRANSCRIPTIONAL CHANGES UPON KNOCKDOWN OF ALTERED *BCOR/BCORL1* TRANSCRIPTS IN PRECLINICAL MODELS OF CNS EMBRYONAL TUMORS WITH BCOR-RELATED ALTERATIONS

Martin Piontek[1,2], Dominik Kirchhofer[2], Lisa Gabler[2,3], Daniela Lötsch-Gojo[4], Christine Pirker[2], Felix Schmitt-Hoffner[5,6], Carola N. Jaunecker[2], Marcel Kool[5,7], Walter Berger[2], Johannes Gojo[1,5]; [1]Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria. [2]Center for Cancer Research and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria. [3]Department of Pediatric Oncology, Dana-Farber Boston Children's Cancer and Blood Disorders Center, Boston, USA. [4]Department of Neurosurgery, Medical