additional cycles of chemotherapy, the MRI showed ≥ 50% reduction in tumor volume and no neurological deficit can be clinically detected. CONCLUSION: This case indicates that stereotactic interstitial brachytherapy during intensive systemic chemotherapy is feasible. It may provide a suitable treatment for malignant infant brain tumors. Furthermore, it shows that paediatric patients are capable of recovery even after devastating neurological symptoms. Lastly, it emphasizes the importance of multidisciplinary and multimodal treatment for rare diseases.

**ETMR-05. SINGLE-CELL TRANSCRIPTOMICS OF ETMR REVEALS DEVELOPMENTAL CELLULAR PROGRAMS AND TUMOR-PERICYTE COMMUNICATIONS IN THE MICROENVIRONMENT**

Flavia W. de Faria[1], Carolin Walter[1,2], Marta Interlandi[1,2], Viktoria Melcher[1], Nicole Riedel[1], Monika Graf[1], Natalia Moreno[1], Melanie Schoof[3,4], Dörthe Holdhof[3,4], Christian Thomas[5], Michael C Frühwald[6], Bruno Maerkl[7], Ben Ho[8], Sarah Sandmann[2], Julian Varghese[2], Martin Ebinger[9,10], Martin Schuhmann[11], Aysegül Canak[9], Annie Huang[12,13], Ulrich Schüller[3,4], Thomas K. Albert[1], Kornelius Kerl[1]; [1]Department of Pediatric Hematology and Oncology, University Children's Hospital Münster, Münster, NRW, Germany. [2]Institute of Medical Informatics, Westphalian Wilhelms-University Münster, Münster, NRW, Germany. [3]Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, HH, Germany. [4]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, HH, Germany. [5]Institute of Neuropathology, University Hospital Münster, Münster, NRW, Germany. [6]Swabian Children's Cancer Center, Paediatric and Adolescent Medicine, University Medical Center Augsburg, Ausburg, Bavaria, Germany. [7]General Pathology and Molecular Diagnostics, Medical Faculty, University of Augsburg, Ausburg, Bavaria, Germany. [8]Department of Cell Biology, Hospital for Sick Children, Toronto, Ontario, Canada. [9]Department Pediatric Hematology/Oncology, Children's University Hospital, Eberhard Karls University of Tuebingen, Tübingen, BW, Germany. [10]German Cancer Consortium (DKTK) partner site Tübingen, Tübingen, BW, Germany. [11]Division of Pediatric Neurosurgery, Department of Neurosurgery, University Hospital of Tuebingen, Eberhard Karls University of Tuebingen, Tübingen, BW, Germany. [12]Division of Haematology Oncology, Department of Paediatrics, Hospital for Sick Children, Toronto, Ontario, Canada. [13]The Arthur and Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children, Toronto, Ontario, Canada

BACKGROUND: Embryonal tumors with multilayered rosettes (ETMR) are pediatric brain tumors bearing a grim prognosis, despite intensive multimodal therapeutic approaches. Insights into cellular heterogeneity and cellular communication of tumor cells with cells of the tumor microenvironment (TME), by applying single-cell (sc) techniques, potentially identify mechanisms of therapy resistance and target-directed treatment approaches. MATERIAL AND METHODS: To explore ETMR cell diversity, we used single-cell RNA sequencing (scRNA-seq) in human (n=2) and murine ETMR (transgenic mode; n=4) samples, spatial transcriptomics, 2D and 3D cultures (including co-cultures with TME cells), multiplex immunohistochemistry and drug screens. RESULTS: ETMR microenvironment is composed of tumor and non-tumor cell types. The ETMR malignant compartment harbour cells representing distinct transcriptional metaprograms, (NSC-like, NProg-like and Neuroblast-like), mirroring embryonic neurogenic cell states and fuelled by neurogenic pathways (WNT, SHH, Hippo). The ETMR TME is composed of oligodendrocyte and neuronal progenitor cells, neuroblasts, microglia, and pericytes. Tumor-specific ligand-receptor interaction analysis showed enrichment of intercellular communication between NProg-like ETMR cells and pericytes (PC). Functional network analyses reveal ETMR-PC interactions related to stem-cell signalling and extracellular matrix (ECM) organization, involving factors of the WNT, BMP, and CxCl12 networks. Results from ETMR-PC co-culture and spatial transcriptomics pointed to a pivotal role of pericytes in keeping ETMR in a germinal neurogenic state, enriched in stem-cell signalling. Drug screening considering cellular heterogeneity and cellular communication suggested novel therapeutic approaches. CONCLUSION: ETMR demonstrated diversity in the microenvironment, with enrichment of cell-cell communications with pericytes, supporting stem-cell signalling and interfering in the organization of the tumor extracellular matrix. Targeting ETMR-PC interactions might bring new opportunities for target-directed therapy.

**ETMR-06. MOLECULAR AND CLINICAL CHARACTERISTICS OF CNS TUMORS WITH *BCOR(L1)* FUSION/INTERNAL TANDEM DUPLICATION**

Johannes Gojo[1,2], Felix Schmitt-Hoffner[2,3], Monika Mauermann[2,3], Katja von Hoff[4], Martin Sill[2,3], Andrey Korshunov[5,6], Damian Stichel[5,6], David Capper[7], Arnault Tauziede-Espariat[8], Pascale Varlet[8], Kenneth Aldape[9], Zied Abdullaev[9], Andrew Donson[10], Jens Pahnke[11], Ulrich Schüller[12], Ivy Tran[13], Kristyn Galbraith[13], Matija Snuderl[13], Sanda Alexandrescu[14], Sebastian Brandner[15], Maria Łastowska[16], Evelina Miele[17], Jasper v. Lugt[18], Lisethe Meijer[18], Jens Bunt[18], Christof Kramm[19], Jordan R. Hansford[20], Lenka Krskova[21], Michal Zapotocky[22], Sumihito Nobusawa[23], David Solomon[24], Christine Haberler[25], Barbara Jones[2,3], Dominik Sturm[2,3], Felix Sahm[2,5], Natalie Jäger[2,3], Stefan M. Pfister[2,3], Marcel Kool[2,18]; [1]Department of Pediatrics and Adolescent Medicine, Comprehensive Cancer Center and Comprehensive Center for Pediatrics, Medical University of Vienna, Vienna, Austria. [2]Hopp-Children's Cancer Center Heidelberg (KiTZ), Heidelberg, Germany. [3]Division of Pediatric Neurooncology, German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany. [4]Department of Pediatric Oncology and Hematology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany. [5]Department of Neuropathology, Heidelberg University Hospital, Heidelberg, Germany. [6]Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany. [7]Department of Neuropathology, Charité Universitätsmedizin, Berlin, Germany. [8]Department of Neuropathology, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, Paris, France. [9]Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. [10]Morgan Adams Foundation Pediatric Brain Tumor Research Program, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA. [11]Department of Pathology, Section of Neuropathology, Translational Neurodegeneration Research and Neuropathology Lab, University of Oslo and Oslo University Hospital, Oslo, Norway. [12]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [13]Department of Pathology, New York University School of Medicine, New York, New York, NY, USA. [14]Department of Pathology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA. [15]Department of Neurodegeneration, Institute of Neurology, University College London, London, United Kingdom. [16]Department of Pathomorphology, The Children's Memorial Health Institute, Warsaw, Poland. [17]Department of Oncology, Hematology, Cell Therapy, Gene Therapy and Haemopoietic Transplant, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy. [18]Princess Máxima Center for Paediatric Oncology, Utrecht, Netherlands. [19]Division of Pediatric Hematology and Oncology, University Medical Center Goettingen, Göttingen, Germany. [20]Department of Oncology and Haematology, Perth Children's Hospital, Perth, WA, Australia. [21]Department of Pathology and Molecular Medicine, Second Faculty of Medicine, Charles University, Prague, Czech Republic. [22]Prague Brain Tumor Research Group, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic. [23]Department of Human Pathology, Gunma University Graduate School of Medicine, Maebashi, Japan. [24]Department of Pathology, University of California, San Francisco, [513] Parnassus Ave, Health Sciences West[451], San Francisco, CA, USA. [25]Institute of Neurology, Department of Neurology, Medical University of Vienna, Vienna, Austria

Central nervous system (CNS) tumor with *BCOR* internal tandem duplication (*BCOR*-ITD) have recently been introduced in the 5th edition of the WHO classification of CNS tumors, however, their molecular makeup and clinical characteristics remain widely enigmatic. This is further complicated by the recent discovery of tumors characterized by gene fusions involving *BCOR* or its homologue *BCORL1*. We identified a cohort of 206 *BCOR* altered CNS tumors via DNA methylation profiling and conducted *in-depth* molecular and clinical characterization in an international effort. By performing t-SNE clustering analysis we found that *BCOR*-fusion tumors form a distinct cluster (n=61), adjacent to *BCOR*-ITD cases (n=145). The identified fusion partners of *BCOR(L1)* included *EP300* (n=20), *CREBBP* (n=5), and *NUTM2HP* (n=1). Notably, three cases within the *BCOR*-ITD cluster harbored a c-terminal intragenic deletion within *BCOR*. With respect to clinical characteristics gender ratio was balanced in *BCOR*-fusion cases (m/f, 1.1), whereas predominance of male patients was observed in the *BCOR*-ITD group (m/f, 1.5). Moreover, age at diagnosis of *BCOR*-fusion patients was higher as compared to *BCOR*-ITD cases (15 vs 4.5 years). Interestingly, *BCOR*-fusion tumors were exclusively found in the supratentorial region being originally diagnosed as ependymomas or gliomas whereas *BCOR*-ITD emerged across the entire CNS with diverse original diagnoses. 8% of *BCOR*-ITD and none of *BCOR*-fusion cases were disseminated at diagnosis. In line with this observation, 40% of first relapses within the *BCOR*-ITD group were metastatic which was less frequent in *BCOR*-fusion tumors. Survival estimates demonstrated no differences, generally showing short median PFS (*BCOR*-fusion, 2 years, n=15; *BCOR*-ITD, 1.8 years, n=55) and intermediate OS rates (*BCOR*-fusion, 6.8 years, n=18; *BCOR*-ITD 6.3 years, n=60). Further molecular and clinical characterization is ongoing potentially revealing first therapeutic leads for these highly aggressive CNS tumor types.

**ETMR-07. DNA METHYLATION PROFILING OF A SERIES OF RARE CNS EMBRYONAL TUMORS IN CHILDREN: DIAGNOSTIC AND CLINICAL IMPACT**

Vito Andrea Dell'Anna, Stefano Gabriele Vallero, Franca Fagioli, Paola Peretta, Paola Cassoni, Luca Bertero; Città della Salute e della Scienza and University of Turin, Turin, Italy

BACKGROUND: CNS embryonal tumors are a clinically and biologically heterogeneous group of tumors, more frequently arising in very young chil-