

additional cycles of chemotherapy, the MRI showed  $\geq 50\%$  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

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**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

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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

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