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ETMR-30. CLINICAL AND MOLECULAR CHARACTERIZATION OF DICER-MUTANT CENTRAL NERVOUS SYSTEM SARCOMA

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BACKGROUND: Central nervous system (CNS) sarcomas are rare mesenchymal non-meningothelial tumors accounting for 0.2% of brain tumors. Due to their rarity, there is a lack of substantive clinical, histological and molecular data. METHODS: Patients diagnosed with primary CNS sarcomas were identified through several international collaborations. DNA methylation profiles were generated using 850K microarray assays, followed by unsupervised hierarchical clustering and t-SNE analyses. Additionally, targeted DNA sequencing was employed to characterize the somatic landscape. Clinical data was collected and summarized using descriptive statistics, and survival estimates were calculated using the Kaplan-Meier method. RESULTS: We analyzed DNA methylation data of 65 tumor samples. Clustering analyses demonstrated DICER-1 CNS sarcomas segregate into two distinct epigenetic subgroups. Copy number analysis demonstrated frequent CNV alterations and chromothripsis in 35% of the samples. DICER-1 mutations were present in 85% of cases and associated with frequent additional alterations in TP53 (65%) and KRAS (51%). The median age at diagnosis was 10.4 years (r: 0.4 - 71 y) and 52% (n=34) of subjects were male. Tumors were frequently (91%) located in the supratentorial compartment, frontal lobe involvement was noted in 62% of cases. Patients were treated with multimodal approaches including surgery, ICE chemotherapy, and focal radiation. At median follow-up time of 27.5 months, the 2-year progression-free and overall survival was 50.8% (r: 0.31-0.67) and 53.5% (r: 0.34-0.69) respectively. CONCLUSIONS: DICER-1 CNS Sarcoma is an aggressive entity that segregates into two epigenetic subgroups, clinical and genotype correlations remain to be elucidated. Current multimodal approaches are only effective in a subset of patients. The identification of MAPK pathway alterations in most cases should be explored as a therapeutic avenue.