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Abstracts

ABSTRACT CATEGORY CODES

ATRT - ATYPICAL TERATOID RHABDOID TUMOR

RARE - CRANIOPHARYNGIOMA AND RARE TUMORS

DIPG - DIFFUSE MIDLINE GLIOMA/DIPG

DDEL - DRUG DELIVERY/PHARMACOKINETICS

EPCT - EARLY PHASE CLINICAL TRIALS

EPCT - EPENDYMOMA

EPID - EPIDEMIOLOGY

ETMR - ETMR AND OTHER EMBRYONAL TUMORS

GCT - GERM CELL TUMORS

HGG - HIGH GRADE GLIOMA

IMG - IMAGING

IMMU - IMMUNOTHERAPY

LGG - LOW GRADE GLIOMA

MEDB - MEDULLOBLASTOMA

NFB - NEUROFIBROMATOSIS AND OTHER PREDISPOSITION SYNDROMES

QOL - NEUROPSYCHOLOGY/QUALITY OF LIFE

SURG - NEUROSURGERY

NURS - NURSING

OTHR - OTHERS (NOT FITTING ANY OTHER CATEGORY

PATH - PATHOLOGY/CLASSIFICATION

LINC - PEDIATRIC NEURO-ONCOLOGY IN LOW/MIDDLE INCOME COUNTRIES

MODL - PRECLINICAL MODELS/EXPERIMENTAL THERAPY/DRUG DISCOVERY

RONC - RADIATION ONCOLOGY

SWK - SOCIAL WORK/PATIENT SUPPORT/PALLIATIVE CARE

TBIO - TUMOR BIOLOGY (NOT FITTING A SPECIFIC DISEASE CATEGORY)

THER - VIRAL/GENE THERAPY AND OTHER NOVEL THERAPIES

INSP - INVITED SPEAKERS

ATYPICAL TERATOID RHABDOID TUMOR

ATRT-01. RECONSTITUTION OF CGAS/ STING PATHWAY VIA EPIGENETIC REPROGRAMMING LEADS TO ANTI-VIRAL INFLAMMATORY SIGNALING IN ATYPICAL TERATOID RHABDOID TUMORS (ATRTS)

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BACKGROUND: Atypical teratoid rhabdoid tumors (ATRTs) are highly aggressive brain tumors that affect young children characterized by biallelic inactivation of the SMARCB1 gene. Though patients benefit from multimodal therapy, there is no improvement in overall survival which necessitates the exploration of alternative approaches. Innate-based immune and epigenetic therapies have shown benefits in several cancers. The role of innate immune signaling has not been investigated in ATRTs. Our previous data from several ATRT cell lines showed loss of expression of key innate signaling components, like cGAS and STING that are needed for sensing extracellular dsDNA. Additionally, ATRT cell lines do not respond to STING agonists, like cGAMP or ISD. RESULTS: Co-treatment of ATRT cell lines, BT-12 and BT-16 with two epigenetic modulators, panobinostat and decitabine, leads to re-expression of cGAS and STING in a time-dependent manner. Furthermore, treatment with decitabine alone leads to demethylation of several CpG sites on the STING promoter and increased expression of STING mRNA. Panobinostat and decitabine co-treatment reconstitute STING-mediated innate signaling, as measured by IRF-3 and STAT1 phosphorylation and production of ISG-15 and IFIT-1 after treatment with cGAMP, a STING agonist. Co-treatment with panobinostat and decitabine also induced expression of antiviral pro-inflammatory chemokines/cytokines in ATRT cell lines, including type III IFN, IL-6, IL-8, IL-28, and IL-29. CONCLUSION: Our data suggest that ATRT cell lines are unresponsive to innate agonists possibly due to the loss of expression of key innate immune components. However, the cGAS/STING pathway is reactivated by epigenetic drugs, specifically the combination of panobinostat and decitabine. This is further potentiated by treating with STING agonists like cGAMP. Combination treatment of ATRT cell lines with panobinostat and decitabine also induced antiviral inflammatory signaling. This response could be a potential treatment modality to inhibit tumor growth and/or mediate cancer immunotherapy in these aggressive tumors.

ATRT-02. NEUROPSYCHOLOGICAL FUNCTION IN INFANT ATYPICAL TERATOID/RHABDOID TUMOR VERSUS LOW-GRADE GLIOMA SURVIVORS REFLECTS TUMOR MALIGNANCY AND MULTIMODAL TREATMENT

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BACKGROUND: Therapy of infants with brain tumors predisposes these patients to increased risks for cognitive sequelae, especially following radiotherapy. Neuropsychological outcome gains importance for those 40-60% of patients with an atypical teratoid/rhabdoid tumor (ATRT) who survive beyond 2 years. Still, reports on cognitive late-effects in children with ATRT are scarce compared to other pediatric brain tumor groups. We analyzed neuropsychological outcome for long-term ATRT-survivors registered in EU-RHAB and infant low-grade glioma (LGG) survivors from the SIOP-LGG 2004-study and LGG-registry. PATIENTS+METHODS: Age at diagnosis of both cohorts was 0-36 months. ATRT-patients (n=13) treated with up to 54Gy radiotherapy (median age 22 months (±7.1)) were evaluated with the "ATRT-Neuropsychology" tool based on SIOPE-BTG QoS-Group recommendations at median 6.8 years (±2.8) after diagnosis. LGG-patients (n=15) treated without radiotherapy (4/15 with chemotherapy) were analyzed with the German "Neuropsychological-Basic-Diagnostic" tool 5.2 years (±0.6)