hibition of Bcl-2, Bcl-XL and Bcl-w. Following the addition of Navitoclax to the combined treatment, SF188 cells, but not KNS42, show a significance reduction in viability compare to the combination treatment. CONCLUSIONS: Our results suggest that zinc may serve as a potentiator of TMZ therapy in pediatric GBM patients and using a second hit with senolytic drug in some cases may be even more beneficial.

HGG-05. REGRESSION OF RECURRENT GLIOBLASTOMA AFTER BORON NEUTRON CAPTURE THERAPY AND CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN A CHILD

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A 6 y/o girl with recurrent multifocal glioblastoma received 3 times of boron neutron capture therapy (BNCT) and chimeric antigen receptor (CAR)–engineered T cells targeting the tumor-associated antigen HER2. Multiple infusions of CAR T cells were administered over 30 days through intraventricular delivery routes. It was not associated with any toxic effects of grade 3 or higher. After BNCT and CAR T-cell treatment, regression of all existing intracranial lesions were observed, along with corresponding increases in levels of cytokines and immune cells in the cerebrospinal fluid, but new lesions recurred soon after the treatment. This clinical response continued for 14 months after the initiation of first recurrence.

HGG-06. REMARKABLE RESPONSE TO BRAF INHIBITOR IN AN INFANT WITH DISSEMINATED DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR (DLGNT)

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INTRODUCTION: Diffuse Leptomeningeal Glioneuronal Tumor (DLGNT) are rare CNS tumors and in infants, they can be lethal. There are several anecdotal reports in infants with low grade gliomas (LGG) with treated with BRAF inhibitors. METHODS: A six-month old baby girl presented with a 2-week history of absent visual contact and vomiting. Imaging revealed a large 4.7 X 4.2 X 2.8 cm suprasellar charismatic region mass and multiple small extra-axial plaques in spinal canal. The child developed significant ascites post VP shunt requiring shunt externalization, extensive protein infusion support and hospitalization for six weeks. Immunohistochemical staining revealed Olig-2 and S-100, GFAP and synaptophysin positive. EMA showed patchy cytroplasmic reactivity in stromal cells and CD99 showed diffuse reactivity in stromal and lesional cells. INI-1, IDH-1, and CD117 were negative. Ki-67 proliferation index was 8–10%. PCR for BRAF V600E/E2/D was detected and KIAA1549-BRAF fusion as negative. This was confirmed by Genome Wide Next Generation Sequencing. While waiting for GNS testing results, the baby received one dose of Vinblastine. However, within seven days of initiating Debrafenib, significant clinical and radiological responses were observed. CONCLUSION: The baby continues safely on Debrafenib with continued dramatic radiological response. This suggest that there may be a role in early initiation of targeted therapy such as *BRAF* inhibitors rather than giving standard chemotherapy such as Vinblastine or Carboplatin-Vincristine in extremely ill infants with low grade gliomas.

HGG-07. CYCLIN-DEPENDENT KINASES AS TARGET STRUCTURES FOR CANCER THERAPY – A COMPARATIVE IN VITRO ANALYSIS ON PATIENT-DERIVED GLIOBLASTOMA CELL CULTURE MODELS

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INTRODUCTION: Current therapeutic approaches have limited clinical success for Glioblastoma patients, making novel strategies urgent. Cyclin-dependent kinases (CDK) are crucial in cell cycle, oncogenic transcription, DNA repair, and stem-cell renewal. Glioma cells frequently show genomic alterations in CDKs. Here, we evaluated the antitumoral activity of selective CDK inhibitors (CDKI) abemaciclib (CDK4/6), palbociclib (CDK4/6), and dinaciclib (CDK1/2/5/9) alone and in combination with chemo-/radiotherapy. MATERIALS/METHODS: Low passage glioblastoma cell lines (N=5) with different molecular characteristics were cultured in 2D and 3D (neurospheroids (NSPs), glioma stem-cells (GSCs). The impact of CDKI alone or in combination with TMZ and radiation (2Gy) was examined. Viability was measured using Calcein-AM and 3D-Glo assays; DNA double-strand breaks by γ-H2AX immunofluorescence. Functional analyses were performed from a 2D culture (72h treatment). RESULTS: Dinaciclib significantly affected viability of GBM cell lines even shortly after low-dose treatment. CDK 4/6 inhibitors were less effective. Abemaciclib and dinaciclib acted radio-sensitizing. Dinaciclib combined with different substances (72h, dose: IC_{20}), synergistically potentiated antitumoral effects. In a scratch assay, abemaciclib decelerated wound healing; dinaciclib even induced cell death. Microarray analysis revealed altered gene expression: Genes mediating cell adhesion, division, DNA-binding, apoptosis (*Casp3*,*Casp8*), senescence (*ASF1A,CENPA,FBXO31*), and autophagy (*ATG4D,ATG2A,SOGA1*) were upregulated. Chemotaxis-mediating *(CXCL8,CCL20)* and proto-oncogenes like *JUNB* and *FOS* were strongly down-regulated. Long-term treatment induced dinaciclib resistance in 1/5 cases, and none abemaciclib-treated cells. This was reversed when dinaciclib was combined with TMZ. CONCLUSION: Our results demonstrate strong anti-GBM activity of dinaciclib and abemaciclib, with additive effects of chemotherapy and radiosensitization, encouraging to move forward this strategy.

HGG-09. FIRST LINE THERAPY OF PEDIATRIC GLIOBLASTOMA WITH LAROTRECTINIB

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PURPOSE: In this case report, we document new recommendations for the treatment of pediatric glioblastoma based on a genetic understanding of the disease. PATIENTS AND METHODS: A Saudi girl aged 18 months presented with a history of right sided weakness and partial seizures. MRI revealed the presence of large complex left frontal tumor. Craniotomy and gross total resection were performed. post-operatively The patient showed excellent recovery with no neurological deficits. Pathology reports confirmed glioblastoma (GBM). Due to the expected poor survival, the patient's family declined standard therapy, including chemotherapy and/or radiation therapy. RESULTS: Molecular analysis showed positive fusion mutations for ETV6-NTRK3 making the patient an ideal candidate for larotrectinib, an oral tyrosine kinase (TRK) inhibitor. Unfortunately, follow-up MRI showed local tumor recurrence at 3-months post-surgery. The family agreed to the initiation of oral larotrectinib as a less invasive therapy. The patient tolerated Larotrectinib very well with no reported side effects. Follow up MRI was performed 8-weeks post-larotrectinib treatment and showed significant tumor regression, indicating an excellent treatment response. CONCLUSION: This case highlights how TRK-inhibitors can be integrated as a first-line therapy for pediatric high grade GBMs harboring TRK-fusions. We also highlight the need for the integration of genomic profiling and molecular analysis into the routine histopathologic analyses of pediatric patients with malignant primary intracranial tumors, to detect any genetic mutations that can be targeted with available therapies to avoid the morbidity associated with non-precision conventional therapies.

HGG-11. HIGH-GRADE GLIOMAS IN ADOLESCENTS AND YOUNG ADULTS HIGHLIGHT HISTOMOLECULAR DIFFERENCES WITH THEIR ADULT AND PAEDIATRIC COUNTERPARTS

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