MAPK pathway has been linked to increased inflammation in several other diseases and holds promise as novel therapy for this disease. Vertical inhibition of the pathway is implicated in glioma tumorigenesis. Drugs targeting this pathway may offer a new strategy for treating gliomas.

Kirsten LGG-46. MEKI WITH MIRDAMETINIB: EXPLORING ADAPTIVE REGIMENS. LGG-45. LOW DOSE CARBOPLATIN – ETOPOSIDE REGIMEN IN HEMISPHERIC TUMORS: A MULTICENTER STUDY. Maria, Maria Luigia, Benedetta, Natalia Muñoz, Lorenzo, Olivia, Anna, Kim, Barbara, Florence, Italy, Albert Einstein College of Medicine, NYC, USA

**INTRODUCTION:** Glial neoplasms are among the most common types of solid tumors in children. The mitogen-activated protein kinase (MAPK) pathway is implicated in glioma tumorigenesis. Drugs targeting this pathway hold promise as novel therapy for this disease. Vertical inhibition of the MAPK pathway has been linked to increased inflammation in several other cancers but similar exploration in pediatric brain tumors is limited. Within the MAPK pathway, MEK plays a significant role as a modulator of ERK phosphorylation. This study investigates the therapeutic potential of the MEK inhibitor, Mirdametinib, and evaluates the drugs’ capacity to induce tumor-intrinsic inflammation by characterizing changes in PD-L1 expression and proliferation in a panel of pediatric glial neoplasms. METHODS: Three cell lines were included in the panel (Res186, Res259, SF188) and were treated with Mirdametinib for 3, 5, or 7 days. P-ERK expression, analyzed by western blot, verified successful inhibition of MEK by Mirdametinib. The CCK8 cytotoxic assay was utilized to determine the drug's 50% inhibitory concentration as well as its direct effects on cell viability. Changes in Ki67 expression assessed by flow cytometry further characterized Mirdametinib's effects on cell proliferation. Flow cytometry was also utilized to measure changes in PD-L1 expression following treatment. RESULTS: Despite minimal effects on proliferation as measured by Ki67 and CCK8, expression of P-ERK verifies successful inhibition of MEK. Western blot data also reveals increased PI3K/AKT pathway activity in SF188 groups treated with Mirdametinib. FACS data for SF188 also demonstrates increased PD-L1 expression in response to treatment. CONCLUSIONS: Data suggests that, in response to MEKis, gliomas utilize compensatory growth mechanisms through PI3K/AKT signaling. Findings also point to immune-modulatory effects of MEKi. Supporting results in ongoing experiments are expected to further our understanding of these mechanisms and may help inform effective combination treatment strategies for pediatric gliomas.

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