BACKGROUND

• High-grade gliomas (HGG) comprise 6-10% of all brain tumors in children but account for the highest number of deaths, with a median survival rate of 15 months.

• Pediatric HGG (pHGG) cure rates range from 20% for supratentorial tumors to 0% for diffuse intrinsic pontine glioma (DIPG).

• pHGG can recur after initial surgical, radiation, and chemotherapy interventions as faster-growing, often metastatic tumors with minimal effective treatment options. Median survival from recurrence is 5 months.

RESULTS

Recurred pHGG samples share a common global RNA expression pattern

Recurred tumors have a common methylation pattern and stem-cell like gene expression pattern

CONCLUSIONS

• Genomic analysis of 8 matched primary and recurrent pHGG tumors identified pathways of recurrence and potential sensitivities targetable with pharmacological agents

• Developed in vitro and PDX in vivo models of recurrence through induction of radiation resistance that showed dedifferentiation phenotype and sensitivity to MEK inhibition

IMPLICATION

• Trametinib and other MEK/MAPK inhibitors may uniquely provide treatment advantages in recurrent pHGG versus primary pHGG and thus could be used as salvage therapy after relapse.

DISCLOSURES/FUNDING

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