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Targeting the RAS/MAPK pathway in children with glioma

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Abstract

Purpose: Pediatric gliomas are the most common brain tumor in children, encompassing both low-grade glioma (pLGG) and high-grade glioma (pHGG). Alterations in the RAS/MAPK pathway are the driver event in the majority of pLGG and account for a subset of pHGG. Identification of these alterations has resulted in the transition to targeted therapy as a treatment option.

Results: In pLGG, multiple trials have demonstrated superior outcomes using targeted therapy compared to traditional chemotherapy regimens. This has transformed care for these patients over the past decade with targeted therapy moving into front-line treatment regimens in certain scenarios. Despite these advances, novel targeted therapy approaches continue to present unique challenges to patient care, including optimal duration of therapy, distinct toxicity profiles and the unknown potential impact on the natural history of disease. While targeted therapy has revolutionized treatment of pLGG, additional questions remain in regard to pHGG including the role of targeted therapy in combination with other treatments, such as chemotherapy/radiation, and mechanisms of resistance. These developments are promising treatment options for pediatrics gliomas, enabling a move towards precision medicine.

Conclusion: Herein, we review the role of RAS/MAPK targeted therapy for treatment of pediatric glioma along with the current controversies and outstanding questions.

Keywords: BRAF inhibitor; FGFR inhibitor; Glioma; MEK inhibitor; Pan-RAF inhibitor.