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Novel therapies for pediatric low grade glioma

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Abstract

Purpose of review: Current biological findings provide new insights into the genetics driving growth of low-grade gliomas in pediatric patients. This has provided new targets for novel therapies. The purpose of this paper is to review novel therapies for pediatric low-grade gliomas that have been published in the past 24 months.

Recent findings: Low-grade gliomas are often driven by mitogen activated protein kinase (MAPK) alterations either with BRAF V600E point mutations or BRAF fusions. Current advances have also highlighted novel fusions of fibroblast growth factor receptor (FGFR), myeloblastosis family of transcription factors (MYB), meningioma 1 tumor suppressor (MN1), neurotrophic receptor kinase family of receptors (NTRK), Kristen RAS (Rat Sarcoma Virus) oncogene homolog in mammals (KRAS), Receptor tyrosine kinase ROS proto oncogene 1 (ROS1), protein kinase C alpha (PRKCA), and platelet derive growth factor receptor (PDGFR) amplification. Novel therapies have been employed and are showing encouraging results in pediatric low-grade gliomas. Current trials are underway with newer generation pan RAF inhibitors and mitogen activated protein kinase - kinase (MEK) inhibitors. Other early phase clinical trials have provided safety data in pediatric patients targeting FGFR fusion, NTRK fusion, PDGFR amplification and ROS1 mutations.

Summary: Historical treatment options in pediatric low-grade gliomas have utilized surgery, radiation therapy and conventional chemotherapy. Recently greater insight into their biology has found that alterations in MAPK driven pathways are often the hallmark of tumorigenesis. Targeting these novel pathways has led to tumor control and shrinkage without the use of conventional chemotherapy. Caution should be taken however, since these treatment options are still novel, and we do not fully appreciate the long-term effects. Nonetheless a new era of targeted medicine is here.