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Immunotherapy for pediatric low-grade gliomas

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Abstract

Pediatric low-grade gliomas (pLGGs) are the most common brain tumor types affecting children. Although gross-total resection remains the treatment of choice, many tumors are not amenable to complete removal, because they either involve midline structures, such as the optic chiasm or hypothalamus, and are not conducive to aggressive resection, or have diffuse biological features and blend with the surrounding brain. Historically, radiation therapy was used as the second-line option for disease control, but with the recognition that this often led to adverse long-term sequelae, particularly in young children, conventional chemotherapy assumed a greater role in initial therapy for unresectable tumors. A variety of agents demonstrated activity, but long-term disease control was suboptimal, with more than 50% of tumors exhibiting disease progression within 5 years. More recently, it has been recognized that a high percentage of these tumors in children exhibit constitutive activation of the mitogen-activated protein kinase (MAPK) pathway because of BRAF translocations or mutations, NFI mutations, or a host of other anomalies that converged on MAPK. This led to phase 1, 2, and 3 trials that explored the activity of blocking this signaling pathway, and the efficacy of this approach compared to conventional chemotherapy. Despite initial promise of these strategies, not all children tolerate this therapy, and many tumors resume growth once MAPK inhibition is stopped, raising concern that long-term and potentially life-long treatment will be required to maintain tumor control, even among responders. This observation has led to interest in other treatments, such as immunotherapy, that may delay or avoid the need for additional treatments. This chapter will summarize the place of immunotherapy in the current armamentarium for these tumors and discuss prior results and future options to improve disease control, with a focus on our prior efforts and experience in this field.

Keywords: Astrocytoma; Immunotherapy; Low-grade glioma; Pilocytic; Pleomorphic xanthoastrocytoma; Vaccines.