Treatment of high-grade glioma in children and adolescents.

Macdonald TJ, Aguilera D, Kramm CM.
Aflac Cancer Center and Blood Disorders Service, Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA, USA (T.J.M., D.A.); University Children's Hospital, Martin Luther University Halle-Wittenberg, Halle, Germany (C.M.K.).

Abstract
Pediatric high-grade gliomas (HGGs)-including glioblastoma multiforme, anaplastic astrocytoma, and diffuse intrinsic pontine glioma—are difficult to treat and are associated with an extremely poor prognosis. There are no effective chemotherapeutic regimens for the treatment of pediatric HGG, but many new treatment options are in active investigation. There are crucial molecular differences between adult and pediatric HGG such that results from adult clinical trials cannot simply be extrapolated to children. Molecular markers overexpressed in pediatric HGG include PDGFRα and P53. Amplification of EGFR is observed, but to a lesser degree than in adult HGG. Potential molecular targets and new therapies in development for pediatric HGG are described in this review. Research into bevacizumab in pediatric HGG indicates that its activity is less than that observed in adult HGG. Similarly, tipifarnib was found to have minimal activity in pediatric HGG, whereas gefitinib has shown greater effects. After promising phase I findings in children with primary CNS tumors, the integrin inhibitor cilengitide is being investigated in a phase II trial in pediatric HGG. Studies are also ongoing in pediatric HGG with 2 EGFR inhibitors: cetuximab and nimotuzumab. Other novel treatment modalities under investigation include dendritic cell-based vaccinations, boron neutron capture therapy, and telomerase inhibition. While the results of these trials are keenly awaited, the current belief is that multimodal therapy holds the greatest promise. Research efforts should be directed toward building multitherapeutic regimens that are well tolerated and that offer the greatest antitumor activity in the setting of pediatric HGG.

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