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Treatment Options for IDH-Mutant Malignant Gliomas

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Abstract

As the peak incidence of isocitrate dehydrogenase (IDH)-mutant gliomas is amongst young adults, there is a need to balance tumor control with long term side effects of therapy. Following initial clinical presentation and acquisition of contrasted diagnostic imaging, tissue diagnosis is essential in suspected diffuse glioma. Depending on the location and extent of disease, maximal surgical resection is preferred both for histologic diagnosis and initial therapy. Partial resection or biopsy alone is considered when the tumor cannot be completely resected or if there are clinical reservations regarding a more significant operation. The classification of diffuse glioma has evolved over time, with histopathology and molecular marker status guiding discussions of prognosis and postoperative management. In patients with IDH-mutant grade 2 glioma and low-risk features, observation with active surveillance is generally recommended following a gross total resection. For those with high-risk features, which historically included age > 40 years or subtotal resection, adjuvant chemotherapy and radiation therapy are generally recommended, however decisions for adjuvant therapy pose challenges as many of the landmark historical trials guiding adjuvant therapy were performed prior to the molecularly defined era. This is an area where multiple clinical trials are ongoing and hold promise to inform treatment paradigms, including recent data on the use of IDH-mutant inhibitors in grade 2 tumors with recurrent or residual disease. For IDH-mutant grade 3 and 4 glioma, adjuvant chemotherapy and radiation are recommended for all patients after initial resection.

Keywords: 1p/19q codeletion; Astrocytoma; Chemotherapy; IDH-mutation; Oligodendroglioma; Radiotherapy.

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