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Chemotherapy for glioblastoma: current treatment and future perspectives for cytotoxic and targeted agents.

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Glioblastoma is the most frequent and devastating primary malignant brain tumor in adults. Surgery followed by standard radiotherapy with concomitant and adjuvant chemotherapy with temozolomide is the standard of care in patients with glioblastoma, however the prognosis remains poor with a median survival in the range of 12-15 months. Common genetic abnormalities in glioblastoma are associated with aberrant activation or suppression of cellular signal transduction pathways and resistance to radiation and chemotherapy. Special attention has been focused on targets such as epidermal growth factor receptor, vascular endothelial growth factor receptor, platelet-derived growth factor receptor, and on pathways such as the phosphatidylinositol-3kinase/Akt/mammalian target of rapamycin and Ras/Raf/mitogen-activated protein-kinase pathways. Several signal transduction inhibitors have been examined in preclinical and clinical malignant glioma trials, including antiangiogenic agents (bevacizumab, enzastaurin), and inhibitors of epidermal growth factor receptor tyrosine kinase (gefitinib and erlotinib), mammalian target of rapamycin (temsirolimus, everolimus) and integrin (cilengitide). Although preliminary clinical results of the use of targeted agents have not translated into significantly better survival, more recent phase II trials are exploring the combination of multitargeted drugs with cytotoxic chemotherapy and radiotherapy in order to overcome the resistance of tumors to single-agent targeted therapies. This review summarizes the current results with cytotoxic and targeted molecular agents in glioblastoma and the development of new chemoradiation strategies under evaluation to increase their effectiveness.

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