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Glioblastoma is both the most common and most aggressive primary brain tumor. Until recently, the standard of care involved maximal safe surgical resection followed by radiation therapy with or without nitrosourea-based chemotherapy. In 2005, the results of a large clinical trial examining the role of adjuvant chemotherapy in management of newly diagnosed glioblastoma were published. This study created a new standard of adjuvant treatment, using concurrent and sequential temozolomide in the initial therapy of glioblastoma. A companion tumor biology study identified the prognostic role of O(6)-methylguanine-DNA methyltransferase (MGMT) status in patients with newly diagnosed glioblastoma. Several preliminary studies have been initiated to address the issue of resistance and suppression of MGMT activity, and have used alternative temozolomide dosing schedules and O(6)-guanine mimetic agents as substrates for MGMT. In addition, recent studies have attempted to define mechanisms responsible for the apparent synergy between temozolomide and radiotherapy. Lastly, an increased understanding of the molecular biology of glioblastoma has provided new leads for the adjuvant treatment of this disease. This Review summarizes new developments in treatment of glioblastoma and speculates on possible future treatment strategies for managing this aggressive cancer.

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