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Localized BCNU chemotherapy and the multimodal management of malignant glioma.

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BACKGROUND: Gliomas account for 42% of all primary CNS neoplasms and 77% of all malignant primary CNS neoplasms. Unfortunately the high-grade variant of gliomas, glioblastoma multiforme (GBM), is difficult to treat and generally considered incurable. Survival rates are generally poor, and neurological morbidity in the setting of disease progression is high. Fortunately, significant progress has been achieved in the past decade in our understanding of the molecular biology of this aggressive tumour histology and, as a consequence, there is renewed clinical trial activity in this area focused on improving quality of life, treatment-related morbidity and outcomes. **METHODS:** A review of literature from June 2005 to June 2008 was conducted on multimodal treatment of malignant glioma (MG) patients, using specific search criteria in Medline, EMBASE, and BIOSIS. Abstracts from relevant US and European medical (cancer) meetings were also evaluated. **RESULTS:** The established therapies for MG include surgery, radiotherapy (RT), and local or systemic chemotherapy. However, over the last 10 years only two chemotherapeutic agents have received regulatory approval for treatment of MG: polifeprosan 20 with carmustine (BCNU implant) and temozolomide (TMZ), an imidazotetrazine derivative of dacarbazine. More recent advances in the treatment of brain tumours have been in the development of multimodal approaches. Specific interest in the combination of BCNU implant and TMZ has arisen due to the demonstrable depletion by TMZ of the DNA repair enzyme responsible for resistance to a nitrosourea such as BCNU. Further interest in this combination stems from the observation that there is a difference in the time to peak effect for each agent. Additional emerging data suggest that multimodal therapy with maximal resection and BCNU implants, followed by adjuvant therapy with radiation and TMZ, is effective and well-tolerated in patients with initial high-grade, resectable MG. **CONCLUSIONS:** The increasing body of efficacy data suggests that this combination of BCNU implants and TMZ within a multimodal treatment strategy including surgery and RT may provide an enhanced benefit compared with the use of either of these agents alone in select patients with high-grade glioma.

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