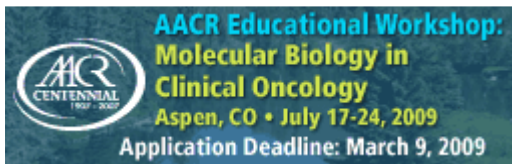


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Clinical Cancer Research Vol. 6, 2585-2597, July 2000
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Minireview

Temozolomide and Treatment of Malignant Glioma¹

Henry S. Friedman², Tracy Kerby and Hilary Calvert

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Malignant gliomas (glioblastoma multiforme and anaplastic astrocytoma) occur more frequently than other types of primary central nervous system tumors, having a combined incidence of 5–8/100,000 population. Even with aggressive treatment using surgery, radiation, and chemotherapy, median reported survival is less than 1 year. Temozolomide, a new drug, has shown promise in treating malignant gliomas and other difficult-to-treat tumors.

Temozolomide, a p.o. imidazotetrazine second-generation alkylating agent, is the leading compound in a new class of chemotherapeutic agents that enter the cerebrospinal fluid and do not require hepatic metabolism for activation. *In vitro*, temozolomide has demonstrated schedule-dependent antitumor activity against highly resistant malignancies, including high-grade glioma. In clinical studies, temozolomide consistently demonstrates reproducible linear pharmacokinetics with approximately 100% p.o. bioavailability, noncumulative minimal myelosuppression that is rapidly reversible, and activity against a variety of solid tumors in both children and adults. Preclinical studies have evaluated the combination of temozolomide with other alkylating agents and inhibitors

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of the DNA repair protein O^6 -alkylguanine alkyltransferase to overcome resistance to chemotherapy in malignant glioma and malignant metastatic melanoma. Temozolomide has recently been approved in the United States for the treatment of adult patients with refractory anaplastic astrocytoma and, in the European Union, for treatment of glioblastoma multiforme showing progression or recurrence after standard therapy. Predictable bioavailability and minimal toxicity make temozolomide a candidate for a wide range of clinical testing to evaluate the potential of combination treatments in different tumor types. An overview of the mechanism of action of temozolomide and a summary of results from clinical trials in malignant glioma are presented here.

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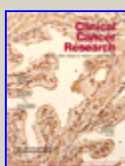
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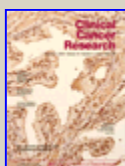
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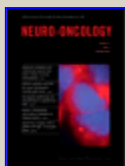
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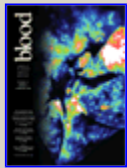
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