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Review

Experience with irinotecan for the treatment of malignant glioma

James J. Vredenburgh ^{1*}, Annick Desjardins ²,
David A. Reardon ², Henry S. Friedman ²

¹ The Preston Robert Tisch Brain Tumor Center at Duke, Duke University Medical Center, DUMC Box 3624, Trent Drive, 047 Baker House, Durham, NC 27710, USA

² Preston Robert Tisch Brain Tumor Center at Duke, Duke University Medical Center, Durham, NC, USA

* To whom correspondence should be addressed. E-mail: vrede001@mc.duke.edu.

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▶ Abstract

Malignant glioma is the most commonly occurring primary malignant brain tumor. It is difficult to treat and usually associated with an inexorable, rapidly fatal clinical course. Chemotherapy, radiotherapy, and surgical excision are core components in the management of malignant glioma. However, chemotherapy, even with the most active regimens currently available, achieves only modest improvement in overall survival. Novel agents and new approaches to therapy are required to improve clinical outcomes. Irinotecan, a first-line treatment for metastatic colorectal cancer and an agent with high activity against solid tumors of the gastrointestinal tract, is an inhibitor of topoisomerase I, a critical enzyme needed for DNA transcription. Irinotecan crosses the blood-brain barrier and, in preclinical investigations, has demonstrated cytotoxic activity against central nervous system tumor xenografts. Its antitumor activity has also been demonstrated against glioblastoma cells with multidrug resistance. Studies in adult and pediatric patients with recurrent, intractable malignant glioma have evaluated irinotecan as monotherapy and in

combination with other agents, including temozolomide, carmustine, thalidomide, and bevacizumab. Studies of irinotecan in combination with other medications, particularly temozolomide and bevacizumab, have yielded promising results. Irinotecan monotherapy has demonstrated efficacy; however, its efficacy appears to be enhanced when it is used in combination with other chemotherapeutic agents. When administered concurrently with enzyme-inducing antiepileptic drugs, the dosage must be increased to compensate for enhanced cytochrome CY3A4/5 enzyme activity. Toxicities associated with irinotecan have been manageable; the most important dose-limiting toxicities are neutropenia and diarrhea. Irinotecan-based chemotherapy of malignant glioma merits further study.

Key Words: EIAEDs, glioblastoma, irinotecan, malignant glioma, SN-38

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