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Regression of Recurrent Malignant Gliomas with Convection-Enhanced Delivery of Topotecan.

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Abstract

BACKGROUND: Convection-enhanced delivery of chemotherapeutics for the treatment of malignant glioma is a technique that delivers drugs directly into a tumor and the surrounding interstitium through chronic, low grade positive-pressure infusion. This allows for high local concentrations of drug while overcoming the limitations imposed by toxicity and the blood-brain barrier in systemic therapies that prevent the use of many potentially effective drugs.

OBJECTIVE: To examine the safety profile of a conventional chemotherapeutic agent, topotecan, via convection-enhanced delivery in the treatment of recurrent malignant gliomas and, secondarily, to assess radiographic response and survival.

METHODS: We performed a prospective, dose-escalation Phase Ib study of the topoisomerase-I inhibitor, topotecan, given by convection-enhanced delivery in patients with recurrent malignant gliomas.

RESULTS: Significant anti-tumor activity as described by radiographic changes and prolonged overall survival with minimal drug-associated toxicity was demonstrated. A maximum tolerated dose was established for future phase II studies.

CONCLUSION: Topotecan by convection-enhanced delivery has significant anti-tumor activity at concentrations that are non-toxic to normal brain. The potential for use of this therapy as a generally effective treatment option for malignant gliomas will be tested in subsequent Phase II and Phase III trials.

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