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Integration of adenovirus thymidine kinase suicide-gene therapy with surgery and radiation therapy for malignant glioma.

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Abstract

Evaluation of: Chiocca EA, Aguilar LK, Bell SD et al. Phase IB study of gene-mediated cytotoxic immunotherapy adjuvant to up-front surgery and intensive timing radiation for malignant glioma. *J. Clin. Oncol.* 29(27), 3611-3619 (2011). This report of a clinical Phase IB trial uses adenoviral vectors injected in a dose escalation manner during surgical excision of primary gliomas to express thymidine kinase and activate the prodrugvalacyclovir, which is administered so as to overlap in part with a standard radiation therapy schedule. The approach aimed to exploit several mechanisms associated with this form of gene therapy, namely tumor cell suicide, radiosensitization and the antitumor immunotherapeutic response that it can activate. The most novel aspect of the trial was the early start to radiation therapy 1 week after surgery that was designed to allow for radiosensitization by orally administered valacyclovir. In general, the treatment was well tolerated and the overall median survival for patients was 12.4 months with a 3-year survival of 25%. There was evidence of immune cell infiltration in all four resection specimens that were examined but no sign of an importance to viral dose within the range of 3×10^{10} - 3×10^{11} particles. This was a small trial with only 13 patients but the results warrant the initiation of further clinical trials to investigate what is now a fairly old but still promising strategy.

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