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Clinical Cancer Research Vol. 10, 5316-5326, August 15, 2004
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Clinical Trials

Clinical Responsiveness of Glioblastoma Multiforme to Chemotherapy after Vaccination

Christopher J. Wheeler, Asha Das, Gentao Liu, John S. Yu and Keith L. Black

Maxine Dunitz Neurosurgical Institute, Cedars-Sinai Medical Center, Los Angeles, California

ABSTRACT

Purpose: Although the development of immune-based therapies for various cancers including malignant glioma has been heralded with much hope and optimism, objective clinical improvements in most vaccinated cancer patients have not been realized. To broaden the search for vaccine-induced benefits, we examined synergy of vaccines with conventional chemotherapy.

Experimental Design: Survival and progression times were analyzed retrospectively in 25 vaccinated (13 with and 12 without subsequent chemotherapy) and 13 nonvaccinated *de novo* glioblastoma (GBM) patients receiving chemotherapy. Immune responsiveness and T-cell receptor excision circle (TREC) content within CD8⁺ T cells (CD8⁺ TRECs) was determined in vaccinated patients.

Results: Vaccinated patients receiving subsequent chemotherapy exhibited significantly longer times to tumor recurrence after chemotherapy relative to

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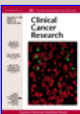
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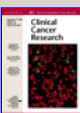
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their own previous recurrence times, as well as significantly longer postchemotherapy recurrence times and survival relative to patients receiving isolated vaccination or chemotherapy. Patients exhibiting objective (>50%) tumor regression, extremely rare in *de novo* GBM, were also confined to the vaccine + chemotherapy group. Prior tumor behavior, demographic factors, other treatment variables, distribution of vaccine responders, and patients with high CD8⁺ TRECs all failed to account for these differences in clinical outcome. Within all GBM patients receiving post-vaccine chemotherapy, however, CD8⁺ TRECs predicted significantly longer chemotherapeutic responses, revealing a strong link between the predominant T-cell effectors in GBM and tumor chemosensitivity.

Conclusions: We propose that therapeutic vaccination synergizes with subsequent chemotherapy to elicit tangible clinical benefits for GBM patients.

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