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[Clin Cancer Res.](#) 2010 Dec 6. [Epub ahead of print]

Gene expression profile correlates with T cell infiltration and survival in glioblastoma patients vaccinated with dendritic cell immunotherapy.

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Abstract

PURPOSE: To assess the feasibility, safety, and toxicity of autologous tumor lysate-pulsed dendritic cell (DC) vaccination and toll-like receptor (TLR) agonists in patients with newly diagnosed and recurrent glioblastoma. Clinical and immune responses were monitored and correlated with tumor gene expression profiles.

EXPERIMENTAL DESIGN: Twenty-three patients with glioblastoma (WHO grade IV) were enrolled in this dose-escalation study and received three biweekly injections of glioma lysate-pulsed DCs followed by booster vaccinations with either imiquimod or poly-ICLC adjuvant every three months until tumor progression. Gene expression profiling, IHC, FACS, and cytokine bead arrays were performed on patient tumors and PBMC.

RESULTS: DC vaccinations are safe and not associated with any dose-limiting toxicity. The median overall survival from the time of initial surgical diagnosis of glioblastoma was 31.4 months, with a one-, two-, and three-year survival rate of 91%, 55% and 47%, respectively. Patients whose tumors had mesenchymal gene expression signatures exhibited increased survival following DC vaccination compared to historical controls of the same genetic subtype. Tumor samples with a mesenchymal gene expression signature had a higher number of CD3+ and CD8+ tumor infiltrating lymphocytes (TILs) compared with glioblastomas of other gene expression signatures ($p = 0.006$).

CONCLUSION: Autologous tumor lysate-pulsed DC vaccination in conjunction with TLR agonists is safe as adjuvant therapy in newly diagnosed and recurrent glioblastoma patients. Our results suggest that the mesenchymal gene expression profile may identify an immunogenic subgroup of glioblastoma that may be more responsive to immune-based therapies.

PMID: 21135147 [PubMed - as supplied by publisher]

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