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# Induction of CD8+ T-Cell Responses Against Novel Glioma-Associated Antigen Peptides and Clinical Activity by Vaccinations With $\alpha$ -Type 1 Polarized Dendritic Cells and Polyinosinic-Polycytidylic Acid Stabilized by Lysine and Carboxymethylcellulose in Patients With Recurrent Malignant Glioma.

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### Abstract

**PURPOSE** A phase I/II trial was performed to evaluate the safety and immunogenicity of a novel vaccination with  $\alpha$ -type 1 polarized dendritic cells ( $\alpha$ DC1) loaded with synthetic peptides for glioma-associated antigen (GAA) epitopes and administration of polyinosinic-polycytidylic acid [poly(I:C)] stabilized by lysine and carboxymethylcellulose (poly-ICLC) in HLA-A2(+) patients with recurrent malignant gliomas. GAAs for these peptides are EphA2, interleukin (IL)-13 receptor- $\alpha$ 2, YKL-40, and gp100. **PATIENTS AND METHODS** Twenty-two patients (13 with glioblastoma multiforme [GBM], five with anaplastic astrocytoma [AA], three with anaplastic oligodendroglioma [AO], and one with anaplastic oligoastrocytoma [AOA]) received at least one vaccination, and 19 patients received at least four vaccinations at two  $\alpha$ DC1 dose levels ( $1 \times$  or  $3 \times 10^7$ /dose) at 2-week intervals intranodally. Patients also received twice weekly intramuscular injections of 20  $\mu$ g/kg poly-ICLC. Patients who demonstrated positive radiologic response or stable disease without major adverse events were allowed to receive booster vaccines. T-lymphocyte responses against GAA epitopes were assessed by enzyme-linked immunosorbent spot and HLA-tetramer assays. **Results** The regimen was well-tolerated. The first four vaccines induced positive immune responses against at least one of the vaccination-targeted GAAs in peripheral blood mononuclear cells in 58% of patients. Peripheral blood samples demonstrated significant upregulation of type 1 cytokines and chemokines, including interferon- $\alpha$  and CXCL10. Nine (four GBM, two AA, two AO, and one AOA) achieved progression-free status lasting at least 12 months. One patient with recurrent GBM demonstrated sustained complete response. IL-12 production levels by  $\alpha$ DC1 positively correlated with time to progression. **CONCLUSION** These data support safety, immunogenicity, and preliminary clinical activity of poly-ICLC-boosted  $\alpha$ DC1-based vaccines.

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