Abstract Number: LB-135

Presentation Title: A pilot study of peptide-based vaccines in combination with poly ICLC in patients with WHO grade 2 low-grade glioma

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Location: McCormick Place West (Hall F), Poster Section 40


Abstract Body: Introduction: Adult patients with WHO grade 2 low-grade glioma (LGG) have a significant risk of tumor progression despite treatment with surgery or surgery followed by radiation therapy (RT) and/or chemotherapy, and most patients eventually die of the disease. High-risk subsets of these LGG patients display astrocytoma or oligoastrocytoma histology plus any one of the following conditions: 1) age $\geq$40 with any extent resection; 2) age 18-39 with incomplete resection; or 3) age 18-39 with neurosurgeon-defined gross total resection with tumor size $\geq$ 4 cm in diameter. These patients have as high as an 89% risk of recurrence by 5 years following surgery.

Methods: Based on encouraging data from a phase I vaccine study targeting multiple glioma-associated antigen (GAA) epitopes in adult high-grade glioma (HGG) patients, we initiated a bi-institutional pilot study of subcutaneous vaccinations of synthetic peptides for GAA epitopes emulsified in Montanide ISA-51 every 3 weeks for 8 courses, and intramuscular administration of poly-ICLC in HLA-A2$^+$ patients with: newly diagnosed high-risk LGG without prior RT (Cohort 1); newly diagnosed high-risk LGG with prior RT (Cohort 2), or recurrent LGG (Cohort 3). Primary endpoints were safety and CD8$^+$ T-cell responses against vaccine-targeted GAAs, assessed by Enzyme-Linked Immuno-SPOT (ELISPOT) assays. Treatment response was evaluated clinically and by MR imaging. Targeted GAAs were EphA2, interleukin (IL)-13 receptor-α2, survivin, and WT1. As these GAAs are expressed not only in a subset of LGG cells but even at higher levels in HGG cells, our vaccine approach may offer both immunotherapeutic and immunoprrophylactic potential to reduce the risk of tumor recurrence.

Results: To date, 13, 1 and 10 patients have been enrolled in Cohorts 1, 2 and 3, respectively. No dose-limiting non-CNS toxicity has been encountered except for one case with Grade 3 fever (Cohort 1). ELISPOT assays, completed in 7 and 1 patients in Cohorts 1 and 2, respectively, demonstrated robust and sustained interferon (IFN)-γ (type-1) responses
against at least 3 of the GAA epitopes in all cases, while IL-5 (type-2) responses were absent or transient in all cases. The magnitude of the IFN-γ ELISPOT responses in the current study was significantly higher than that observed in our previous phase I/II study in HGG patients (Okada H et al. 2011). Although evaluation of progression-free survival would require a longer observation period, among 9, 1 and 7 patients who completed the 8 vaccinations spanning 24 weeks, 6, 1 and 3 patients in Cohorts 1, 2 and 3, respectively, are currently with stable disease.

Conclusion: Our preliminary results demonstrate that the regimen in these patients is well tolerated, and induces robust type-1 anti-GAA T-cell responses. These data suggest that patients with LGG are suitable for vaccine therapy.