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Presentation Title: Peptide vaccine therapy for childhood gliomas: interim results of a pilot study

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Abstract Body: **Introduction:** Malignant astrocytomas of the brainstem and cerebral hemispheres and multiply recurrent low-grade gliomas carry a poor prognosis despite current treatments, and new therapeutic approaches are needed. Having gained significant experience with immunotherapy for adult gliomas, we extended these insights to childhood gliomas, based on our observations regarding their profiles of glioma-associated antigen (GAA) expression.

**Methodology:** We initiated a pilot trial of subcutaneous vaccinations with peptides for GAA epitopes emulsified in Montanide-ISA-51 given every 3 weeks for 8 courses along with intramuscular injections of poly-ICLC in HLA-A2+ children with newly diagnosed brainstem gliomas (BSG), cerebral high-grade gliomas (HGG), or recurrent gliomas. GAAs were EphA2, IL13Rα2, and survivin. Primary endpoints were safety and T cell responses against vaccine-targeted GAAs, assessed by ELISPOT and tetramer analysis. Treatment response was evaluated clinically and by MR imaging.

**Results:** To date, 24 children have been enrolled, 13 with newly diagnosed BSG, 5 with newly diagnosed HGG, and 6 with recurrent gliomas. No dose-limiting non-CNS toxicity has been encountered. One child with a BSG had transient tumor enlargement in association with acute neurological deterioration 4 months after beginning vaccination that later regressed and culminated in a sustained partial response (PR), consistent with pseudoprogression. Two other children with BSG had symptomatic pseudoprogression, with transient neurological deterioration and tumor enlargement followed by stabilization on decreasing steroid doses. Among 22 patients evaluable for response, 4 had rapidly progressive disease, 14 had stable disease for > 3 months, 2 had PRs, 1 had an MR, and 1 had prolonged disease-free status after surgery. ELISPOT analysis, completed in seven children, showed response to IL13Rα2 in 5, EphA2 in 3, and survivin in 3.

**Conclusion:** Peptide vaccination in children with gliomas is generally well tolerated, and has preliminary evidence of both immunological and clinical activity. Pseudoprogression can initially be difficult to distinguish from true tumor progression and aggressive management may be warranted.