Peptide vaccine shows evidence of immunological, clinical activity in children with gliomas

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Peptide vaccination in children with gliomas was well tolerated with evidence of immunological and clinical responses, but some children experienced periods of immunological pseudoprogression, where tumors appeared larger than they actually were, according to results presented at the AACR Annual Meeting 2012, held here March 31 – April 4.

“We’ve found that the vaccine is tolerated well with limited systemic toxicity, but we’ve also observed that there are some patients who have immunological responses to the vaccine target in the brain that can cause swelling and transient worsening, and subsequently, some of those children can have very favorable responses,” said Ian F. Pollack, M.D., Walter Dandy professor of neurological surgery and vice chairman for academic affairs in the department of neurological surgery at the University of Pittsburgh School of Medicine in Pittsburgh, Pa. “We’ve also demonstrated immunological responses in the majority of the kids.”

In the pilot study, Pollack, who is also chief of pediatric neurosurgery at Children’s Hospital of Pittsburgh and co-director of the University of Pittsburgh Cancer Institute Brain Tumor Program in Pittsburgh, Pa., and colleagues enrolled 27 children, including 16 with newly diagnosed brain stem gliomas, five with newly diagnosed cerebral high-grade gliomas and six with recurrent gliomas.

Researchers assigned HLA-A2–positive children to subcutaneous

vaccinations with peptides for glioma-associated antigen (GAA) epitopes emulsified in Montanide-ISA-51 every three weeks for eight courses. They also administered intramuscular injections of poly-ICLC. The GAAs included EphA2, IL13Rα2 and survivin.

Among 22 evaluable cases, four children had rapidly progressive disease, 14 had stable disease for more than three months, three had sustained partial responses and one had prolonged disease-free status after surgery. ELISPOT analysis, which was completed in seven children, revealed responses in six children: to IL13Rα2 in five cases, EphA2 in three and survivin in three.

“These kids, who, for the most part, have intact and very robust immune systems, seem to mount an immune response against the vaccine very effectively at rates that may be even higher than have been noted in studies in adults,” Pollack said.

Pseudoprogression occurred in some cases and was similar to true tumor progression. For example, one child with a brain stem glioma had transient tumor enlargement and acute neurological deterioration four months after vaccine initiation. However, the tumor later regressed and the patient experienced a sustained partial response. Three other children with brain stem gliomas had symptomatic pseudoprogression, with transient neurological deterioration and tumor enlargement followed by stabilization on decreasing steroid doses.

“This was the first study of its type that examined peptide vaccine therapy for children with brain tumors like this,” Pollack said. “The fact that we’ve seen tumor shrinkage in children with very high-risk tumors has been extremely encouraging and somewhat surprising.”

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