[News * Analysis * Commentary * Controversy]

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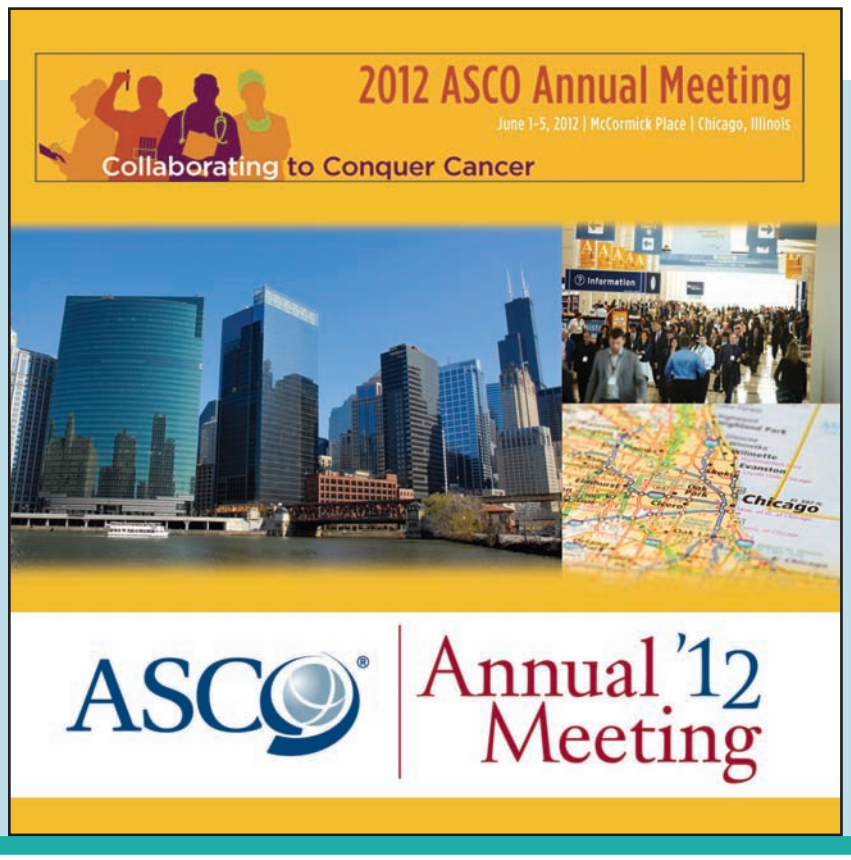

ASCO Annual Meeting!

Collaboration, Personalized Medicine, & the Latest Meeting Technology

BY SARAH DIGIULIO

Previews of the meeting, June 1-5 in Chicago, from ASCO President Michael Link, incoming President-Elect Clifford Hudis, Scientific Committee Program Chair Ronald Levy, and Education Committee Chair Harold Burstein.

PLUS Mikkael Sekeres on how he prepares for the meeting.

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Highlights from the AACR Annual Meeting
pp.15, 16, 19, 20, 21, 42

ASH's Picks for the Top Hematologic Research Areas
p. 18

[ALSO]

PERIODICALS

Glioma: Pilot Trial Shows Peptide Vaccine Active in Pediatric Patients

BY RABIYA S. TUMA, PHD

CHICAGO—Preliminary data suggest that immunotherapies may be a valuable tool for the treatment of gliomas in adults, and now, researchers at the University of Pittsburgh School of Medicine report that a peptide vaccine is also well tolerated and active in children with gliomas. Of 22 pediatric patients evaluable, 19 have had stable disease lasting three or more months or a partial response, according to data presented here at the American Association for Cancer Research Annual Meeting (***Abstract LB-131***).

"Immunological and clinical activity—in some cases very dramatic—has been obtained, and more extensive analysis of safety and efficacy are warranted in a multi-institutional setting," said lead author Ian F. Pollack, MD, the Walter Dandy Professor and Vice Chairman for Academic Affairs in the Department of Neurological Surgery at the University of Pittsburgh School of Medicine, as well as Chief of Pediatric Neurosurgery at Children's Hospital of Pittsburgh and Co-Director of the University of Pittsburgh Cancer Institute Brain Tumor Program.

"These results look very promising," agreed Olivera Finn, PhD, Distinguished Professor and Chair of Immunology, also at the University of Pittsburgh School of Medicine, but not involved in the work.

> The vaccine includes peptides from three proteins that are highly expressed on many gliomas—IL-13Rα2, EphA2, and surviving—as well as the tetanus toxoid helper peptide.

Pollack and colleagues designed the current single-institution study, which was sponsored by the National Institutes of Health, to test the efficacy and safety of the novel vaccine, which includes peptides from three proteins that are highly expressed on many gliomas—IL-13Rα2, EphA2, and surviving—as well as the tetanus toxoid helper peptide. Patients received the vaccine and a co-administered poly-ICLC adjuvant every three weeks for eight courses.

A total of 24 patients enrolled in the trial, including 13 with newly diagnosed brain stem gliomas, five with newly diagnosed high-grade gliomas, three with recurrent low-grade gliomas, and three with recurrent high-grade gliomas. To be eligible for the trial, patients had to be HLA-A2+ and one of the following histologies, glioblastoma, gliosarcoma, or anaplastic astrocytoma.

Phil McCarten/AACR 2012

IAN F. POLLACK, MD: "We've already written a protocol that will advance this vaccine to a Phase II study within the Pediatric Brain Tumor Consortium and, subsequently, within the Children's Oncology Group. So the plan is to advance this to a multi-institutional setting."

Side Effects

In terms of safety, the most common side effects were low-grade flu-like symptoms and mild injection site reactions. There were no Grade 3 or 4 adverse events. However, seven patients developed pseudo-progression, which is a transient enlargement of tumor and neurological worsening. Those who needed treatment for pseudo-progression responded to corticosteroid treatment.

Pseudo-progression appears to be an efficacy signal, but also "a real concern that warrants close monitoring and in many cases intervention," Pollack said.

Of the 22 patients currently evaluable, three had partial responses, one patient had a minor response, one had prolonged disease-free status after resection, and 14 had stable disease. Two patients who were taken off the vaccine due to pseudo-progression had dramatic regressions after starting corticosteroids, Pollack reported.

When asked about the possibility that the corticosteroids might lessen the value of the vaccine, Finn, who moderated a news conference at the meeting that highlighted newsworthy abstracts on vaccines and immunotherapy, acknowledged that it would be preferable if corticosteroids were not needed.

"It would be better not to have side effects that require that treatment," she said. "The hope is that by the time steroids are used, the [immune] cells that arrived to the site of the tumor have done what we were hoping to make them do: kill tumor cells, make useful anti-tumor cytokines, and change the balance in the tumor in favor of anti-tumor responses."

Although the pilot trial was not designed to assess the vaccine's impact on overall survival, Pollack noted that eight of the 11 patients with brain stem gliomas had survived beyond the historical median for this disease, which is about 10.5 months. And many of the patients remain on therapy.

In terms of immunological responses, the investigators have found positive results in 11 out of 13 patient samples tested with ELISPOT assays. Of those, nine patients had antibodies that recognized IL-13Rα2, six had antibodies that recognized EphA2, and seven had antibodies that recognized survivin. Moreover, five out of five tumor samples tested expressed at least one of the antigens included in the vaccine.

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

"We have reached our objective in terms of defining feasibility and safety," Pollack said. However, the team is still enrolling patients in some strata of the trial. Additionally, they are trying to better understand pseudo-progression and define imaging correlates of response to see if they can come up with an imaging-based platform that can be used in a cooperative group trial.

"We've already written a protocol that will advance this [vaccine] to a Phase II study within the Pediatric Brain Tumor Consortium and, subsequently, within the Children's Oncology Group," he said. "So the plan is to advance this to a multi-institutional setting."