Final Results of the Phase II/III Trials of the E75 Adjuvant Breast Cancer Vaccine

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We have completed phase I/II clinical trials vaccinating breast cancer patients with E75, a HLA-A2/A3-restricted HER2/neu (HER2) peptide vaccine. The vaccine was administered in the adjuvant setting to prevent recurrence in high-risk patients rendered disease-free with standard of care therapy. We have previously reported preliminary results indicating that the vaccine (including booster inoculations) is safe, well-tolerated, and effective in stimulating an anti-tumor immune response. Here, we report the final 5 year results from these trials.

RESULTS

195 patients were enrolled, 6 withdrew (2 from VG, 4 from CG), 1 was lost to follow-up during the trial, with booster inoculations being offered every 6 months after completion of the PVS. Patients were monitored for local and systemic toxicity (graded by NCI Common Terminology Criteria for Adverse Events). Pre- and post-PVS, in vivo immune response was assessed in the VG by delayed type hypersensitivity (DTH) reactions to both E75 and saline, VG and CG pits were followed for 60 months and recurrences were documented. Demographic differences were compared with the Fisher’s exact test and disease-free survival (DFS) was determined using the Kaplan-Meier method and compared by log-rank test.

CONCLUSIONS

The E75 breast cancer vaccine is safe and well-tolerated. It elicits strong immune responses in vaccinated patients. At the end of the 5 year follow-up period, the E75 vaccine shows a strong trend toward preventing breast cancer recurrences in vaccinated patients. To evaluate this vaccine (now known as NeuVax) further, the PRESENT trial, a prospective, randomized, double-blind, placebo-controlled, multi-center phase III registration trial has been initiated and is actively enrolling.

DISCLOSURE

Dr. Peoples has inventor rights to E75. This vaccine has been licensed for commercial development based on clinical trial results. He is entitled to financial proceeds associated with this license per Federal policy. Dr. Peoples also consults in the development of the vaccine. All other authors have no relevant financial disclosures.

REFERENCES

We refer to the methods section for a detailed description of the trial design and procedures.

METHODS

The phase II/III trials were performed as dose-escalation/schedule-optimization trials enrolling node positive and high-risk, node negative breast cancer patients with tumors expressing any level of HER2 expression. HLA-A2/A3+ patients were enrolled into the vaccine while HLA-A2/A3- patients were followed prospectively as the untreated control group (CG). The VG patients were given 4 monthly intradermal inoculations of E75 with GM-CSF during the primary vaccine series (PVS). In addition, a voluntary booster program was initiated during the trial, with booster inoculations being offered every 6 months after completion of the PVS. Patients were monitored for local and systemic toxicity (graded by NCI Common Terminology Criteria for Adverse Events). Pre- and post-PVS, in vivo immune response was assessed in the VG by delayed type hypersensitivity (DTH) reactions to both E75 and saline, VG and CG pits were followed for 60 months and recurrences were documented. Demographic differences were compared with the Fisher’s exact test and disease-free survival (DFS) was determined using the Kaplan-Meier method and compared by log-rank test.