Primary analysis of the prospective, randomized, single-blinded phase II trial of AE37 vaccine versus GM-CSF alone administered in the adjuvant setting to high-risk breast cancer patients.

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Abstract:

Background: AE37 is the Ii-Key hybrid of the HER2 peptide AE36 (HER2 aa:776-790). It is a MHC class II epitope capable of stimulating CD4+ helper T-cells. We have completed accrual to a prospective, randomized, multi-center, phase II trial of the AE37 vaccine for prevention of breast cancer recurrence. Here the planned primary analysis of disease free survival (DFS) is presented.

Methods: The trial randomized clinically disease-free, node positive or high-risk node negative patients (pts) with any level of HER2 expression to receive AE37 + GM-CSF (VG) or GM-CSF alone (CG) following standard of care therapy. Pts received 6 monthly intradermal inoculations during the primary vaccine series (PVS) followed by four boosters administered every 6 months. Statistical analysis was performed in the following groups: intention-to-treat (ITT) as the entire randomly assigned trial population, HER2 non-overexpressing (nOE) pts with IHC 1/2+ or FISH- tumors regardless of ER/PR status, and triple negative breast cancer (TNBC) pts with HER2 nOE and ER/PR tumors. Results: With 298 pts (VG= 153, CG= 145) enrolled, there are no differences between groups with respect to age, rate of node positivity, tumor grade, tumor size, ER/PR status, and HER2 over-expression (all p > 0.05). The vaccine is safe and well tolerated with no grade 3 local toxicities and 1 pt experiencing grade 3 systemic toxicity. DFS analyses by Kaplan Meier demonstrated a 12% relative reduction in recurrence (RRR) in the ITT population (19/153 v 20/145 events; HR(CI) 0.89 (0.47, 1.66), p=0.70), a 40% RRR in HER2 nOE pts (10/76 v 14/78 events; HR(CI) 0.60 (0.26, 1.35), p=0.21), and 60% in TNBC pts (4/25 v 9/25; HR(CI) 0.40 (0.12, 1.32), p=0.12). Conclusions: AE37 + GM-CSF is a novel vaccine that is safe and well tolerated with minimal toxicity. The primary analysis of this prospective, randomized, single-blinded phase II trial demonstrates benefit in patients with HER2 nOE tumors, especially those with triple negative tumors. These data justify a phase III trial evaluating AE37 administered in the adjuvant setting to a HER nOE or specifically TNBC population. Clinical trial information: NCT00524277.