**METHODS**

The phase I/II trials were performed as dose escalation/schedule optimization trials enrolling HLA-A2/A3+, node positive and high-risk, node-negative patients with tumors expressing any level of HER2. HLA-A2/A3- patients were followed as controls. Vaccinated patients were given 4-6 monthly inoculations of E75 with GM-CSF. The vaccine has been studied in the adjuvant setting to prevent recurrences in clinically disease-free patients after completion of standard therapy. We have previously reported that the vaccine is safe, effectively stimulates HER2-specific immunity, and appears to improve disease-free survival at 24 months. Here, we report long-term data at a median follow-up of 60 months.

**RESULTS**

187 patients were enrolled; 108 in the vaccine group (VG) and 79 in the unvaccinated control group (CG). The vaccine and control groups were well-matched with the only statistically significant difference being ER-/PR- status (31.1% in VG vs 17.7% in CG, p=0.04). Vaccination was well tolerated with primarily grade 1 and grade 2 toxicity in the PVS (Local Toxicity: 85% Grade 1, 15% Grade 2, 0% Grade 3; systemic toxicity: 71% Grade 1, 14% Grade 2, and 3% Grade 3) (Figure 3). Fifty-three of the VG patients received at least one booster, with 34 receiving a second booster, 25 a third, 22 a fourth, 12 a fifth, and 9 receiving at least six boosters. Booster inoculations were well-tolerated with only grade 1 and 2 local and systemic toxicities (Figure 2). There were delayed urticarial reactions in 7/53 (13%) of the boosted patients occurring at a median of 9 days (5-21 days) after inoculation; these were grade 2 reactions and well-tolerated. After a median follow-up of 60 months, there has been a non-significant increase in the Disease Free Survival (DFS) observed in the VG compared to the CG (10.6% vs 20.3%, p=0.098) (Figure 3). The hazard ratio is 0.52 in the VG. In patients with immunity maintained with voluntary boosters, DFS is improved to 95.9% (p=0.016) (Figure 3).

**DISCUSSION**

The E75 breast cancer vaccine is safe and well-tolerated even with prolonged booster inoculations. With long-term follow-up at 60 months, the E75 vaccine continues to show a strong trend toward preventing breast cancer recurrence in vaccinated patients particularly in patients whose immunity is maintained with booster inoculations. To investigate this further, a phase III trial with prospective boosting is being initiated.