Pre-specified interim analysis in a prospective, randomized phase II trial of trastuzumab vs trastuzumab + NeuVax to prevent breast cancer recurrence in HER2+ breast cancer patients

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INTRODUCTION

The HER2-targeted monoclonal antibody, trastuzumab, is standard of care for HER2-positive breast cancer and has been shown to reduce recurrence. We have previously shown that NeuVax (E75 peptide + GM-CSF), a HER2-targeted peptide vaccine, is safe, immunogenic, and may have synergistic clinical efficacy when combined with trastuzumab. Given the known cardiac toxicity of trastuzumab, there is concern that adding a HER2-directed vaccine to trastuzumab therapy may exacerbate this effect. We are currently enrolling patients in a multi-center, prospective, randomized, single-blinded, placebo-controlled phase II trial combining trastuzumab and Neuvax in the adjuvant setting to prevent recurrence in HER2+ breast cancer patients. Here, we present the initial safety data.

Figure 1: Vaccination Timeline

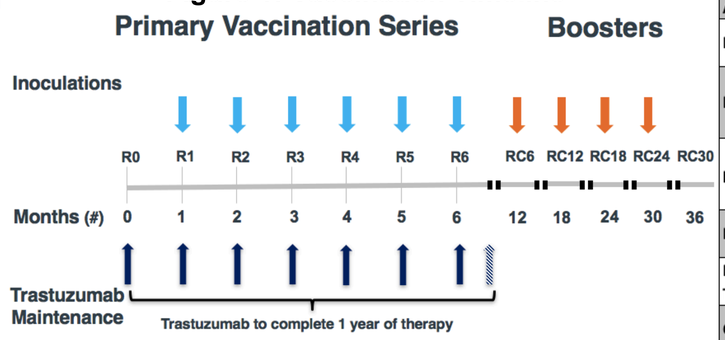


Table 1: Demographics		VG (n=22)	CG (n=28)	*p* value
Age (median)		48.0	56.3	0.137
Race	White	14 (63.6%)	20 (71.4%)	0.169
	Non-white	8 (36.4%)	8 (28.6%)	
Histology	Ductal	16 (72.7%)	22 (78.6%)	0.638
	Lobular	2 (9.1%)	2 (7.1%)	
	Other	4 (18.2%)	4 (14.3%)	
pAJCC Stage	I	1 (4.5%)	7 (25%)	0.474
	II	10 (45.5%)	10 (35.7%)	
	III	11 (50%)	11 (39.3%)	
Breast Surgery	Mastectomy	18 (81.8%)	21 (75.0%)	0.563
	Lumpectomy	4 (18.2%)	7 (25.0%)	
Prior Trastuzumab	Adjuvant	5 (22.7%)	5 (17.9%)	0.669
	Neoadjuvant	17 (77.3%)	23 (82.1%)	
Chemotherapy	Anthracycline	5 (22.7%)	6 (21.5%)	0.618
	No Anthracycline	17 (77.3%)	22 (78.5%)	

Figure 2: Related Toxicity by Grade

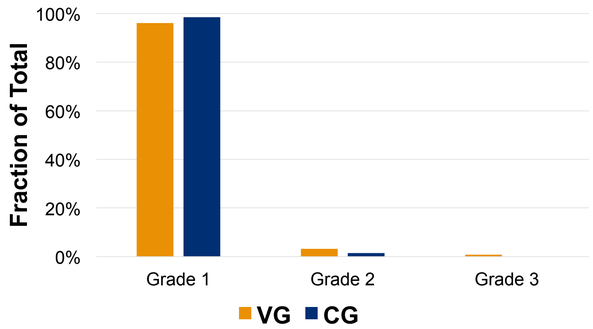
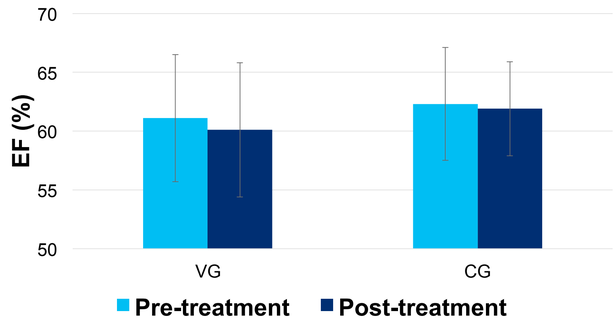


Figure 3: Pre- and post-treatment EF



RESULTS

To date, we have enrolled 50 patients (VG n=22, CG n=28). There were no significant clinicopathologic differences between groups (**Table 1**). There were no related grade 4 or 5 toxicities and no differences in related toxicities between the VG and CG (Grade 1: 96% vs 98.5%; Grade 2: 3.2% vs 1.5%; Grade 3: 0.8% vs 0%, *p*=0.14; **Figure 2**). There was no significant reduction in EF pre- to post-treatment in either group (VG: 61.1±5.4% vs 60.1±4.8%, p=0.55; CG: 62.3±5.7% vs 61.9±4.0%, *p*=0.74; **Figure 3**) and there was no difference in change between groups (p=0.54).

METHODS

HLA-A2/A3+ breast cancer patients with stage I-III HER2+ disease at high risk for recurrence (patients not achieving complete response after trastuzumab-containing neoadjuvant therapy or those undergoing up-front surgery with any node-positive disease if ER/PR- or ≥4 positive nodes if ER/PR+) were enrolled after surgery, radiation and neo-adjuvant/adjuvant chemotherapy with approved trastuzumab-containing regimen. Patients were randomized to receive trastuzumab + NeuVax in the vaccine group (VG) or trastuzumab + GM-CSF only in the control group (CG). Patients received vaccinations of NeuVax or GM-CSF intradermally every 3 weeks for 6 total vaccinations (primary vaccine series, PVS) starting with the third dose of trastuzumab maintenance therapy. Starting 6 months after the completion of the PVS, patients received 4 booster inoculations, one every 6 months (**Figure 1**). Cardiac ejection fraction (EF) was assessed by either echo or MUGA at baseline and serially during treatment. Demographic and safety data were collected and analyzed. Safety analysis was initiated after enrollment of the 50th patient.

CONCLUSIONS

- Combination of trastuzumab and Neuvax in HER2+ breast cancer patients is well tolerated
- The cardiac affects from trastuzumab are not worsened by the addition of NeuVax
- Goal enrollment of 100 patients in this ongoing trial, with immunologic and clinical outcomes data to be reported at planned primary analysis after 24-months follow-up.

Disclosures: Dr. George E. Peoples, M.D. serves as a consultant to Galena Biopharma in the development of the vaccine.