Completed SN33 Trial: 60 month Follow-up of Early Stage Node Positive HER2 Negative Patients with NeuVax™ (E75) and Sargramostim

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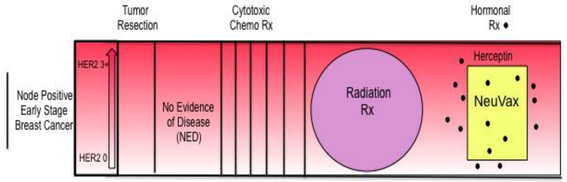
Background

Despite recent advances in adjuvant treatment, some HER2 negative patients still relapse. Unlike HER2 positive patients, the benefit of Herceptin® has not been shown in HER2 negative patients. Here we present the final 60-month results of a Phase 1/2 clinical trial vaccinating early stage node-positive breast cancer patients with NeuVax™ (E75, nelipepimut-S) and sargramostim following adjuvant chemotherapy and radiation. Patients were treated at Walter Reed Army Medical Center and the Windber Medical Center.

Methods

Eligible patients had excised early stage node-positive breast cancer with any level of HER2 expression. After completion of standard of care chemotherapy and radiation, patients were enrolled but not randomized: patients were assigned to the vaccine group (VG) only if they were HLA A2+ or A3+. The non-treated patients were followed as a control group (CG). Hormone receptor positive patients received appropriate adjuvant therapy concomitant with vaccine.

NeuVax therapy follows standard of care resection, chemotherapy, radiation for node-positive invasive breast cancer patients.



The Phase 1/2 trial was performed with Phase 1 as a dose escalation/schedule optimization where VG was given 3-6 monthly inoculations of NeuVax (E75, nelipepimut-S) with the immunoadjuvant, sargramostim. The Phase 2 portion utilized the optimal dose and schedule carried forward. Herceptin® became commercially available during the conduct of the trial, and HER2 positive patients were offered this treatment but remained on trial. DFS was summarized by Kaplan-Meier life tables and analyzed by the log-rank test.

Boosters Added by Amendment:

Due to waning immunity after the scheduled monthly vaccinations, a voluntary booster program was initiated to be integrated into the trial process.

Results

NeuVax: Phase 1/2 Baseline Characteristics SN-33

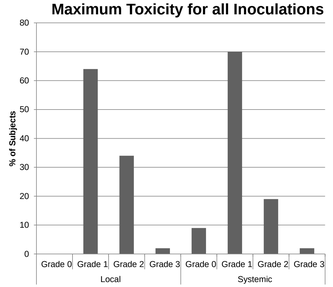
	Vaccinated, HLA-A2+, A3+ (n=53)	Observed, HLA-A2-, A3- (n=44)	*P*
Median age, years	52	49	
Range, years	27-72	31-83	0.15
Tumor size			
T2-T4	46%	60%	0.16
Histological grade			
Grade III	55%	44%	0.31
Median + nodes (NP only)	2.0	2.5	
Range	1-15	1-25	0.22
Her2/neu IHC 3+ or FISH+	32%	39%	0.50
Chemotherapy	98%	95%	0.43
XRT	81%	84%	0.70
Hormonal Therapy	74%	77%	0.67
Adjuvant Herceptin	19%	7%	0.08

Safety

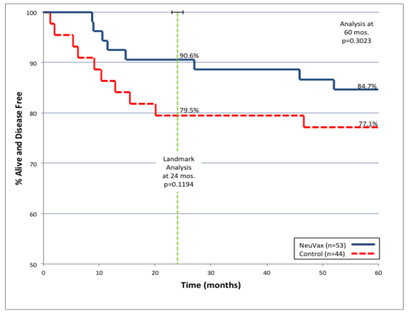
SN-33 Combined: Safety Table (1% or more) (n=108)

Treatment-Related Adverse Events	NP Study (n=246)*
Injection site red/indurated	218 (88.6%)
Fatigue	51 (20.7%)
Localized Pruritis (injection site)	50 (20.3%)
Headache	18 (7.3%)
Myalgias	23 (9.3)%
Bone pain	16 (6.5%)
Malaise	5 (2.0%)
Arthralgias	13 (5.3%)
Back pain	12 (4.9%)
Nausea	7 (2.9%)
Chills	5 (2.0%)
Diarrhea	4 (1.6%)
Fever	6 (2.4%)
Tongue hypersensitivity	7 (2.9%)
Flu-like Symptoms	2 (0.8%)
Facial flushing	0 (0%)
Neck Pain	3 (1.2%)
Injection site bruising	3 (1.2%)
Injection site swelling	3 (1.2%)
GERD	3 (1.2%)

Maximum Toxicity for all Inoculations

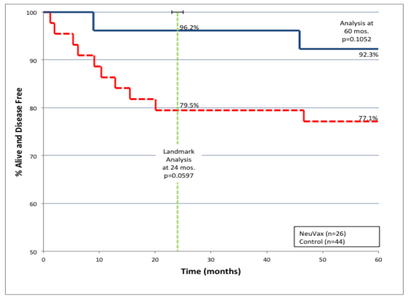


SN-33 Phase 1/2 Intent to Treat (N=97)



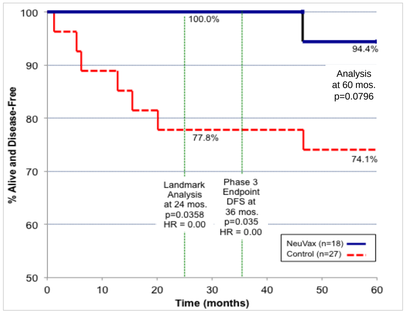
ITT patients in this phase 1/2 trial favored VG in DFS at 24 months (VG 90.6%, CG 79.5%, p=0.1194); at 60 months, the VG continues to have fewer recurrences than the CG (VG 84.7% vs. 77.1%)

SN-33 Phase 2 Intent to Treat (N=70)



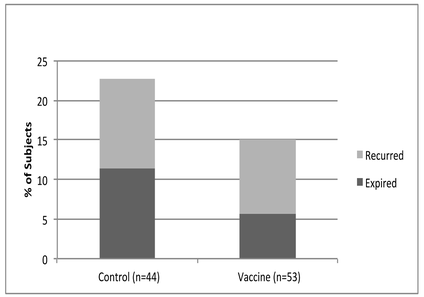
In the patients who were treated at the optimum (Phase 2) dose, the difference in the DFS at 24 months observed was (VG 96.2%, CG 79.5%, p=0.0597); at 60 months, the VG continues to have fewer recurrences than the CG (92.3% vs. 77.1%).

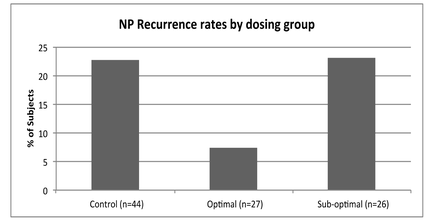
SN-33 Phase 2 HER2 Negative (N=45)

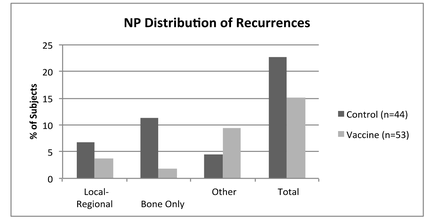


When the HER2 positive patients were removed from the population, the Phase 2 HER2 Negative VG had a significantly improved DFS at 24 months (100% vs. 77.8%, p=0.035); at 60 months, VG retains a 20.3% difference (VG 94.4% vs. CG 74.1%).

Mortality Among Recurrence

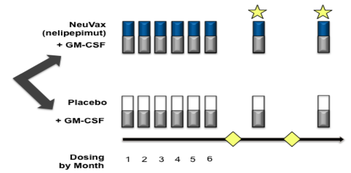






Conclusions

NeuVax (E75, nelipepimut-S) and sargramostim vaccine is safe and well–tolerated in early stage breast cancer patients. With follow-up at 60 months, the vaccine used as adjuvant therapy continues to reduce relapses in node positive HER2 negative patients treated at an optimal dose. A phase 3 multicenter, multinational double-blind trial is underway.



Disclosures

Rosemary Mazanet and Mark Schwartz are employed by Galena Biopharma, Inc. Dunia Ramadan and Phil Lavin are employed by Aptiv Solutions.