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Final analysis of Nelipepimut-S plus GM-CSF with trastuzumab versus GM-CSF with trastuzumab to prevent recurrences in high-risk, HER2 low-expressing breast cancer: a prospective, randomized, blinded multicenter phase IIb trial

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CVDP
CANCERVACCINE
DEVELOPMENT PROGRAM

Disclosures

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of San Antonio Military Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, Department of Defense, or the US Government.

EAM: served on a scientific advisory board for SELLAS

GEP: has partial inventor rights to nelipepimut-S. Patents have been licensed from the US Government for commercial development, and is entitled to financial proceeds associated with this license, per federal policy

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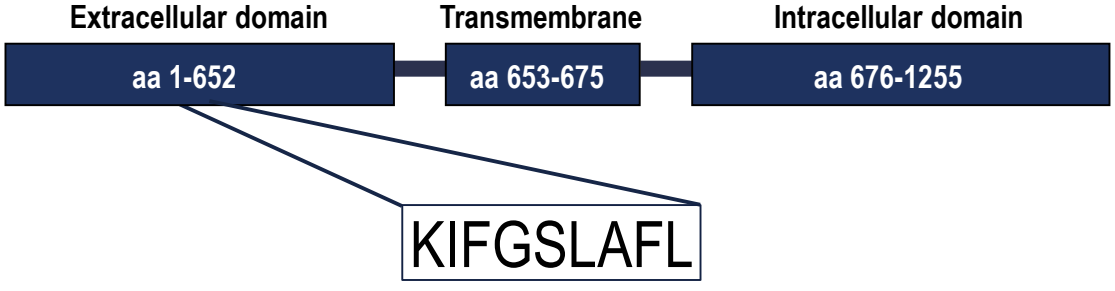
Background

- Patients with HER2 low-expressing breast cancer (IHC 1–2+) are not eligible for adjuvant trastuzumab, approximately 60-70% of patients
- NSABP B-47 confirmed trastuzumab does not improve outcomes in HER2 low-expressing breast cancer[1]

1. Fehrenbacher L, et al. SABCS 2017. Abstract GS1-02.

The HER-2/*neu* peptide vaccine: Nelipepimut-S



Nelipepimut-S

(NeuVax, E75 + GM-CSF)

aa 369-377

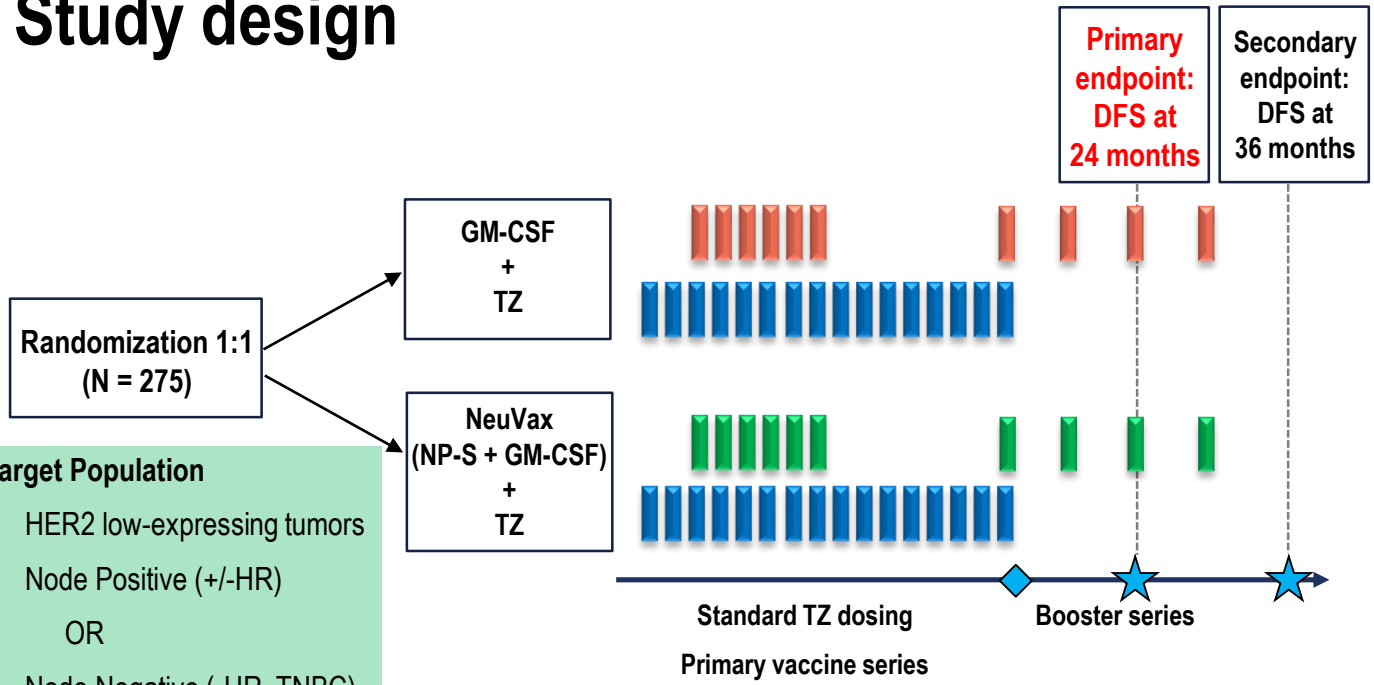
MHC Class I: HLA-A2+, A3+, A24+, A26+

Designed to stimulate CD8 T cells

- Nelipepimut-S + GM-CSF (NeuVax)[1]
  - Safe
  - Immunogenic profile
  - Suggested clinical efficacy
- Preclinical and translational data strongly suggest potential synergy between trastuzumab and a HER2-targeting CD8+ T-cell–eliciting vaccine[2]

1. Mittendorf EA, et al. *Ann Oncol.* 2014;25:1735-1742; **2.** Gall VA, et al. *Cancer Res.* 2017;77:5374-5383.

Study design



Target Population

- HER2 low-expressing tumors
- Node Positive (+/-HR)

  OR
- Node Negative (-HR, TNBC)

Other secondary endpoints

- Safety
- Cardiac toxicity
- Immunologic response

- **This trial investigates whether a combination of trastuzumab and nelipepimut-S can prevent disease recurrence in patients with HER2 low-expressing tumors**

Key inclusion criteria

- Women ≥18 years
- High-risk invasive breast cancer with HER2 expression of 1–2+ by IHC
  - Node Positive (+/-HR)

  OR
  - Node Negative (-HR, thus TNBC)
- Clinically disease free after receiving standard- of-care therapies
- HLA-A2, A3, A24, or A26 positive

Assessments

- Local and systemic toxicity
- Cardiac toxicity
- Immunologic in vivo response
- Disease-free survival

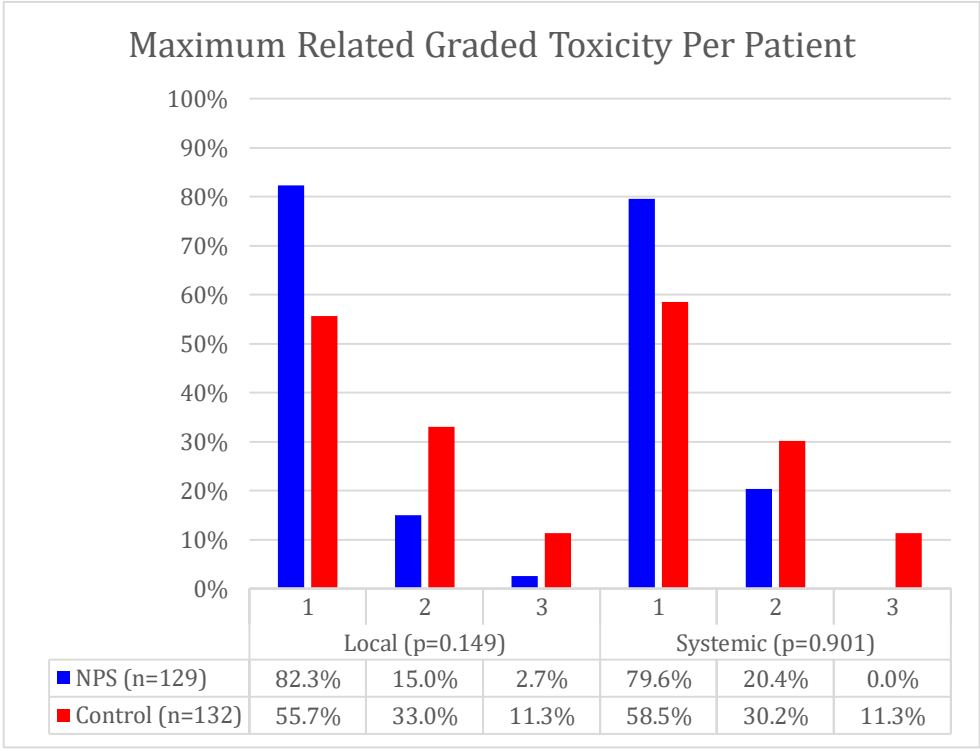
Demographics (ITT)

Characteristics	NeuVax + TZ (N = 136)	TZ (N = 139)	*P* value
Age, years Median (IQR)	52.2 (43.7-60.8)	50.5 (42.0-59.0)	.38
Race, n (%) White Non-white Unknown	 109 (80) 25 (18) 2 (2)	 97 (70) 38 (27) 4 (3)	.20
Chemotherapy Adjuvant Neoadjuvant None	 59 (43) 72 (53) 5 (4)	 57 (41) 76 (55) 6 (4)	.904
Clinical NeoAdj stage, n (%) 0 I II III IV Unknown	 0 (0) 4 (6) 35 (49) 31 (43) 1 (1) 1 (1)	 1 (1) 3 (4) 31 (40) 40 (52) 0 (0) 2 (3)	.334
Path NeoAdj stage, n (%) 0 I II III Unknown	 5 (7) 11 (15) 28 (39) 27 (38) 1 (1)	 4 (5) 9 (12) 26 (34) 37 (49) 0 (0)	.757

Characteristics	NeuVax + TZ (N = 136)	TZ (N = 139)	*P* value
Path (no NeoAdj) stage, n (%) I II III	 10 (16) 26 (41) 28 (44)	 9 (14) 26 (41) 28 (45)	.985
ER status Positive Negative	 81 (60) 55 (40)	 94 (68) 45 (32)	.164
PR status Positive Negative	 77 (57) 59 (43)	 82 (59) 57 (41)	.69
Surgery Yes No	 136 (100) 0	 138 (99) 1 (1)	.638
Radiotherapy Adjuvant Neoadjuvant None	 109 (80) 8 (6) 19 (14)	 122 (88) 2 (1) 15 (11)	.092
Hormone therapy Yes No Other	 73 (54) 61 (45) 2 (1)	 83 (60) 51 (37) 5 (4)	.248

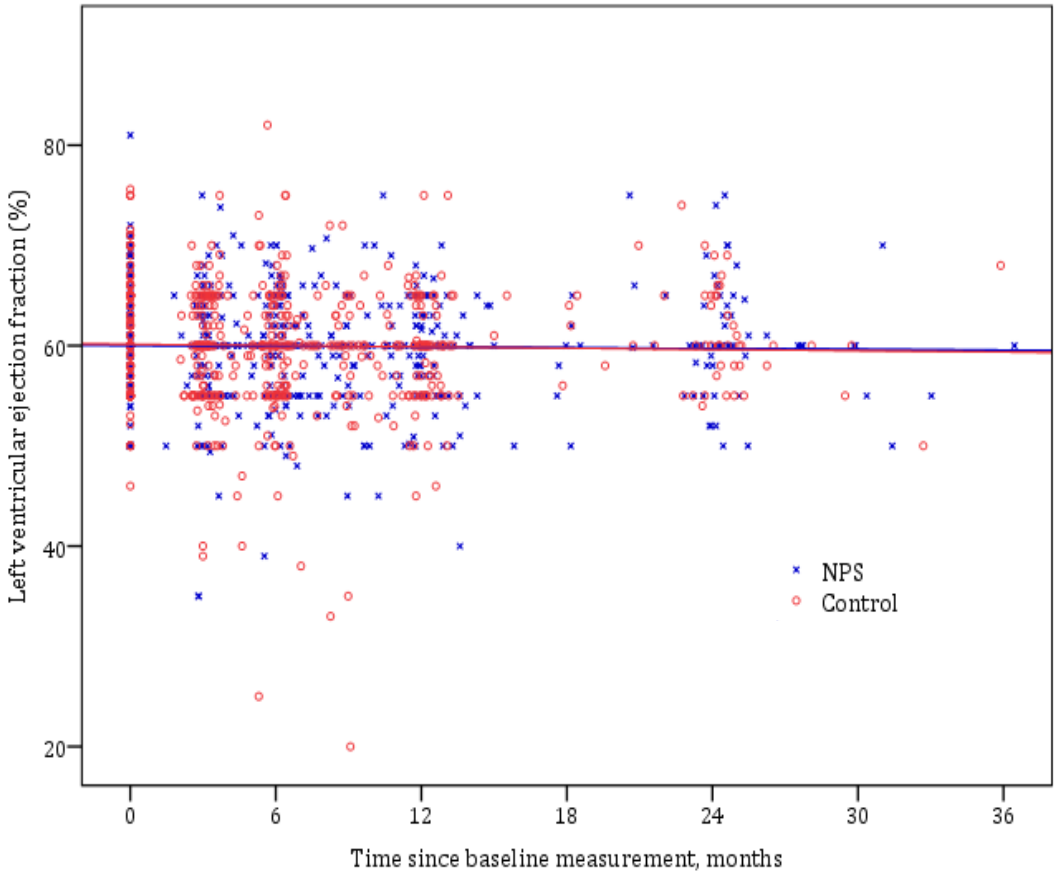
Safety: Treatment-related adverse events

- 94.3% (246/261) of patients who received an intervention experienced at least 1 TRAE
  - No difference between groups (p =0.17)
- Majority of TRAEs were grade 1 or 2
  - Local injection site reactions, skin induration, pruritus, and fatigue



Safety: Cardiac toxicity

- No difference between treatment arms in cardiac ejection fraction over time (*P* = 0.65) and at each time point
- The addition of NeuVax to trastuzumab did not result in any additional cardiotoxicity compared with trastuzumab alone



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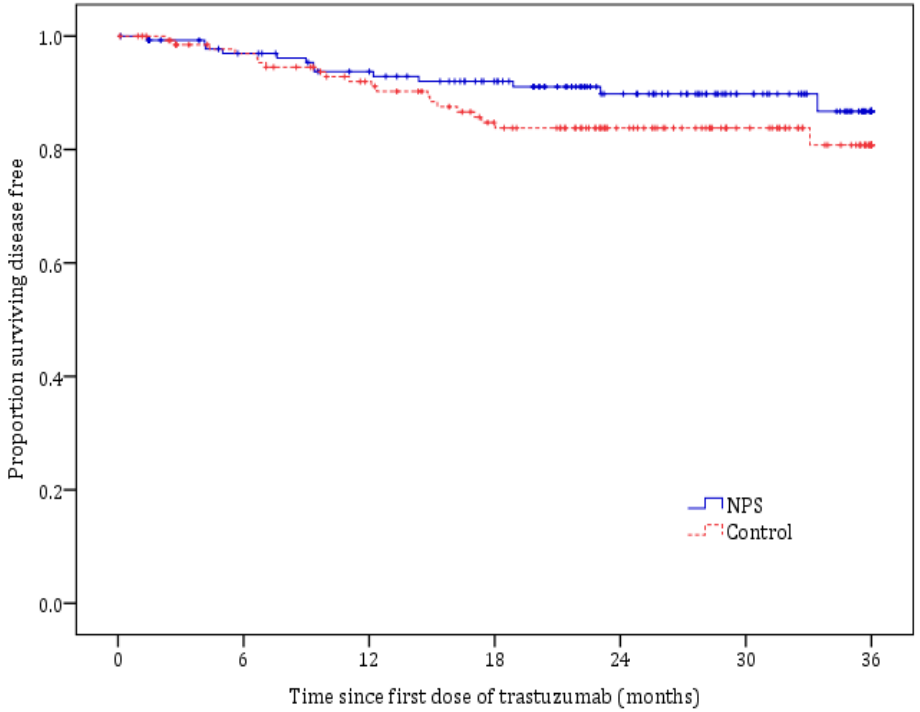
Recurrences

Population	NeuVax + TZ recurrence/total (%)	TZ recurrence/total (%)	*P* value
ITT – All pts	12/136 (8.8)	20/139 (14.4)	0.18
ITT – TNBC pts	4/53 (7.5)	13/44 (26.7)	0.01

Disease-free survival: ITT population



NeuVax + TZ (N = 136)

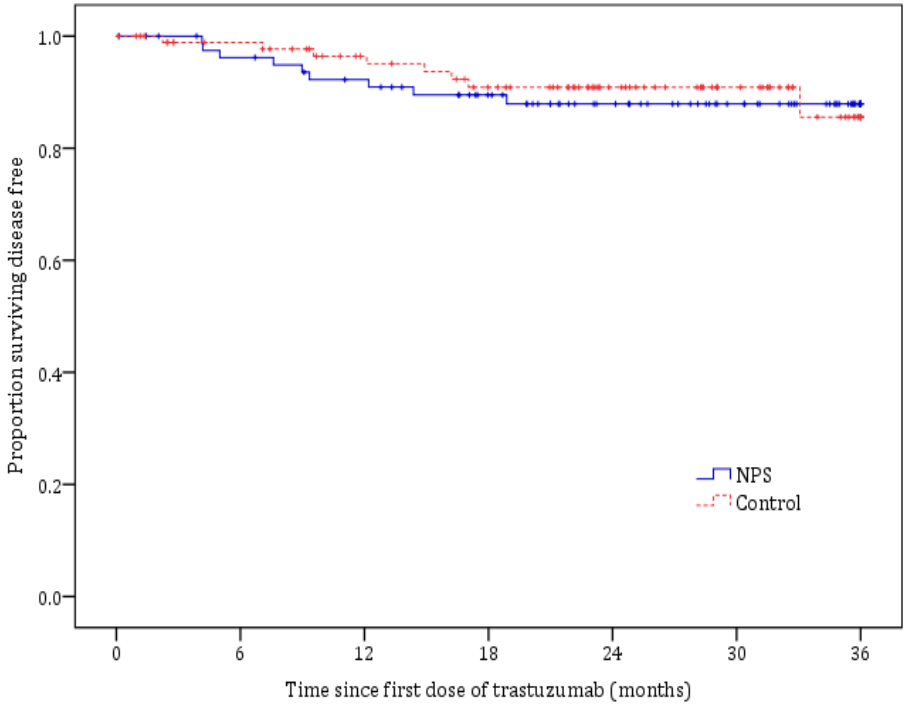
- 36-month DFS = 86.7%
- 24-month DFS = 89.8%

TZ (N = 139)

- 36-month DFS = 80.8%
- 24-month DFS = 83.8%

Median follow-up 24.7 (IQR 18.7–32.7) months
***P* value = 0.18**
Hazard ratio (HR) = 0.62 (CI 0.31–1.25)

Disease-free survival: HR+ patients



NeuVax + TZ (N = 83)

- 36-month DFS = 87.9%
- 24-month DFS = 87.9%

TZ (N = 95)

- 36-month DFS = 85.5%
- 24-month DFS = 90.9%

Median follow-up 25.4 (IQR 18.3–32.8) months
***P* value = 0.71**
HR = 1.19 (CI 0.46-3.01)

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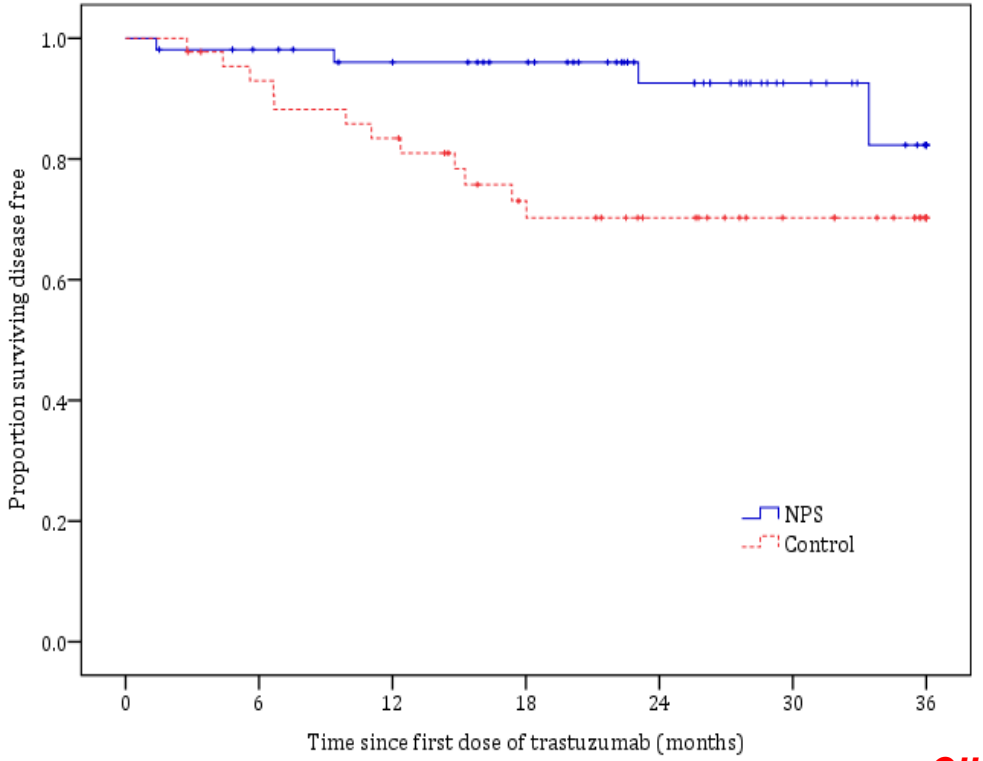
NO difference in median DFS between groups.

DFS comparable with the NSABP B-47 trial (89%).

Disease-free survival: TNBC patients



NeuVax + TZ (N = 53)
- 36-month DFS = 82.3%
- 24-month DFS = 92.6%

TZ (N = 44)
- 36-month DFS = 70.2%
- 24-month DFS = 70.2%

Median follow-up 26.1 (IQR 19.9–31.9) months
***P* value = 0.013**
Hazard ratio = 0.26 (CI 0.08-0.81)

Clinically meaningful and statistically significant difference in median DFS in favor of the combination arm

Conclusions

- The NeuVax + trastuzumab combination is safe; no notable differences between treatment arms
  - No added cardiac toxicity
- NeuVax + trastuzumab may provide clinically meaningful benefit to patients with HER2 low-expressing breast cancers
- The NeuVax + trastuzumab combination demonstrated a statistically significant improvement in DFS in patients with TNBC.
- A future confirmatory phase 3 study in this underserved population with high risk of recurrence and death is warranted
- The sponsor is actively seeking regulatory input by the FDA and EMA