PHASE 2B CLINICAL DATA OF NELIPEPIMUT-S PLUS TRASTUZUMAB IN BREAST CANCER

OCTOBER 22, 2018
8:00 A.M. EDT/ 2:00 P.M. CET

MUNICH 2018 ESMO congress

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This presentation contains forward-looking statements. You can identify such forward-looking statements by the use of the words "expect," "believe," "will," "anticipate," "estimate," "plan," "project" and other words of similar import. The forward-looking statements in this presentation include, but are not limited to, statements related to the results of clinical studies and as to further development of nelipepimut-S (NPS; NeuVax) for breast cancer. These forward-looking statements are based on current plans, objectives, estimates, expectations and intentions, and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with immune-oncology product development and clinical success thereof, the uncertainty of regulatory approval, and other risks and uncertainties affecting SELLAS and its development programs, as set forth under the heading "Risk Factors" in Exhibit 99.1 in its Current Report on Form 8-K filed on July, 18, 2018 and in its other filings with the Securities and Exchange Commission. Other risks and uncertainties of which SELLAS is not currently aware may also affect SELLAS' forward-looking statements. The forward-looking statements herein are made only as of the date hereof. SELLAS undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

NELIPEPIMUT-S (NPS): GENERAL BACKGROUND

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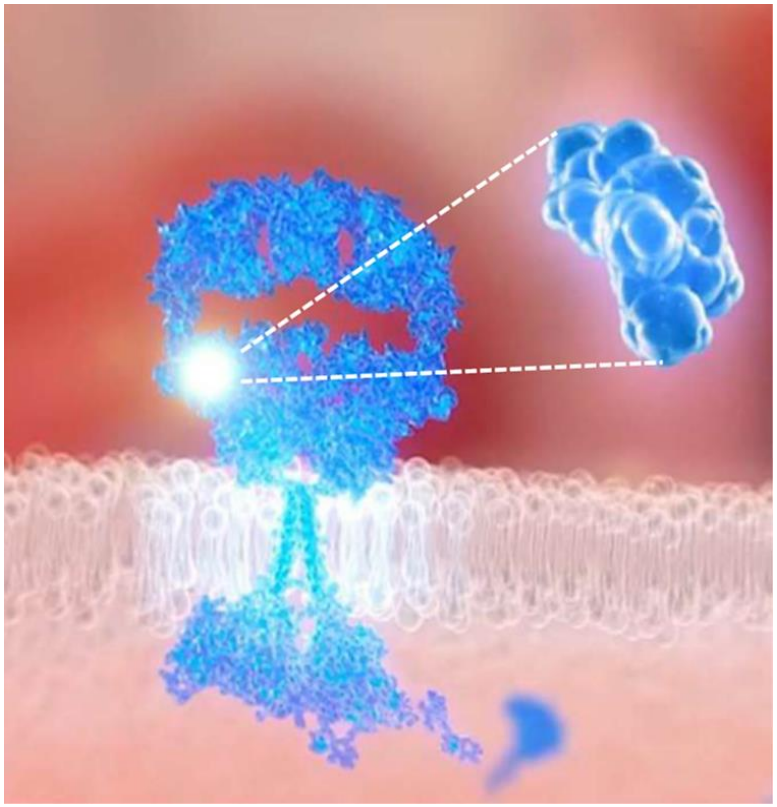
NELIPEPIMUT-S: STIMULATES T-CELL ACTIVITY AGAINST HER2-EXPRESSING CELLS

- Nelipepimut-S (NPS) contains the immunodominant peptide derived from the extracellular domain (ECD) of the HER2 protein
  - NPS is a major histocompatibility complex (MHC) class I epitope which stimulates a CD8+ CTL response
  - This epitope exhibits maximal antigenicity and immunogenicity vs other epitopes along the sequence of the EDC of the HER2 antigen
- NPS induces a de novo highly specific anti-HER2 immune response, which stimulates production of antigen (E75)-specific CD8+ cytotoxic T lymphocytes (CTLs)
- Administered as intradermal injection with GM-CSF[1] (Leukine®) as an adjuvant; the combination of NPS + GM-CSF is historically referred to as nelipepimut-S or NeuVax™



1. *GM-CSF: Granulocyte-macrophage colony-stimulating factor*

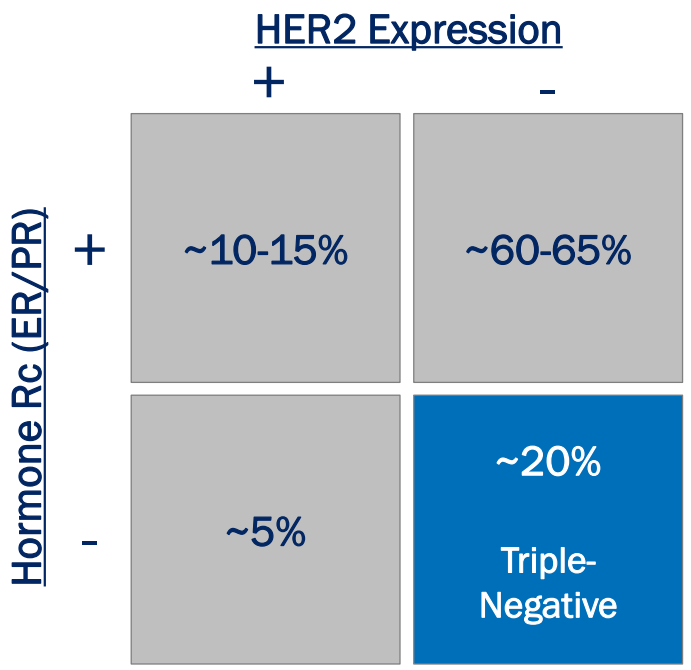
TRIPLE-NEGATIVE BREAST CANCER IS AN UNADDRESSED DISEASE

- **Triple-negative breast cancer applies to tumors that lack the expression of ER, PR and amplification of HER2, which are therefore non-amenable to therapy with agents targeting these molecular moieties (i.e., hormone receptor and HER2 signaling modulators)**

- Estimated annual incidence of ~30K patients in the U.S. and ~268K patients worldwide
- Exhibits poor disease-free interval in the adjuvant setting, shortened progression-free survival and overall survival in the metastatic setting, and a lack of recognized molecular targets for therapy
  - TNBC has a significantly lower survival rate - 78.6% 5-year survival rate for TNBC vs. 90.0% for overall BC
  - Recurrence rate of ~36% at 3 years

TNBC is diagnosed through assessment of ER and PR protein expression levels by immunohistochemistry (IHC), and of HER2 by IHC and/or fluorescence in situ hybridization (FISH)

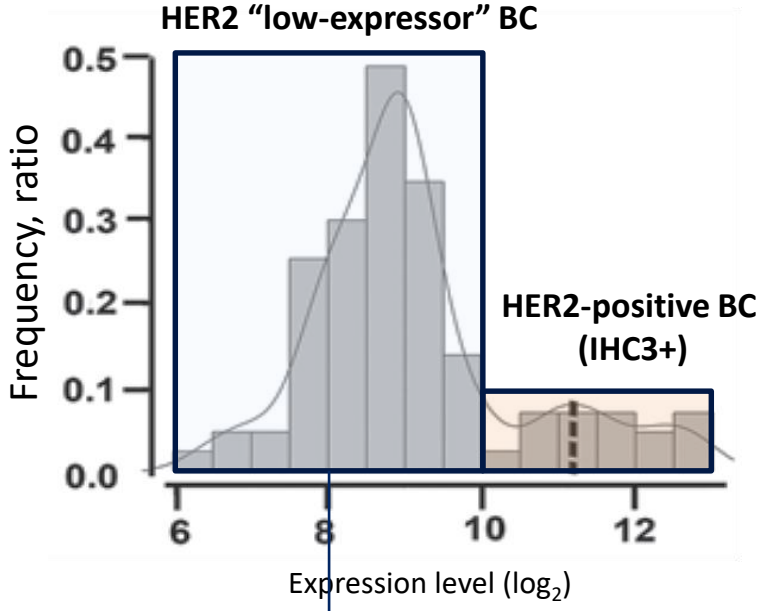
Prevalence in Breast Cancer



HER2 IS A CHALLENGING TARGET WHEN NOT "OVEREXPRESSED"

HER2 Is Still Detectable in High-Frequency in BC but at Much Lower Abundance vs. "Classically" HER2-Positive (IHC 3+) Tumors

HER2 EXPRESSION LEVELS BY FREQUENCY



- HER2 expression is not binary but a range and, as measured by IHC, can be scored on a 0 to 3+ scale
  - Expression can be detected in essentially all BC cells (incl. those of TNBC tumors)

HER2 IHC Expression	Breast Cancer Prevalence	Approved Treatments
3+	15–20%	Multiple
2+	55–65%	None
1+		None
0	Not being evaluated	

Lehman BD, et al. J Clin Invest. 2011;121:2750-2767.

Note: 3+ / 1-2+ HER2 expression is defined by a FISH ratio >2.0 / <2.0, respectively. HER2 IHC scores correspond to the following:

- *1+: Incomplete membrane staining that is faint/barely perceptible in >10% of invasive tumor cells*
- *2+: Circumferential membrane staining that is incomplete and/or weak in >10% of invasive tumors cells, or complete and circumferential intense membrane staining in <10% of invasive tumor cells*
- *3+: Homogenous, dark, circumferential pattern in >10% of invasive tumor cells*

HER2 OVEREXPRESSION MAY FACILITATE IMMUNE ESCAPE

- There is a significant inverse correlation between the expression of HER2 and total MHC class I (HLA-A, -B, and -C) surface expression
  - It has been shown that HER2 over-expressing tumors (IHC 3+) are more prone to escape from HLA-A2 restricted CTLs
  - Low-expressing tumors (IHC 1+/2+) are predictably devoid of that escape and, therefore, more visible to the adaptive immune system, especially after anti-HER2 vaccination

Inverse correlation between HER2 and MHC class I expression levels ($p = 0.031$, χ^2 test)

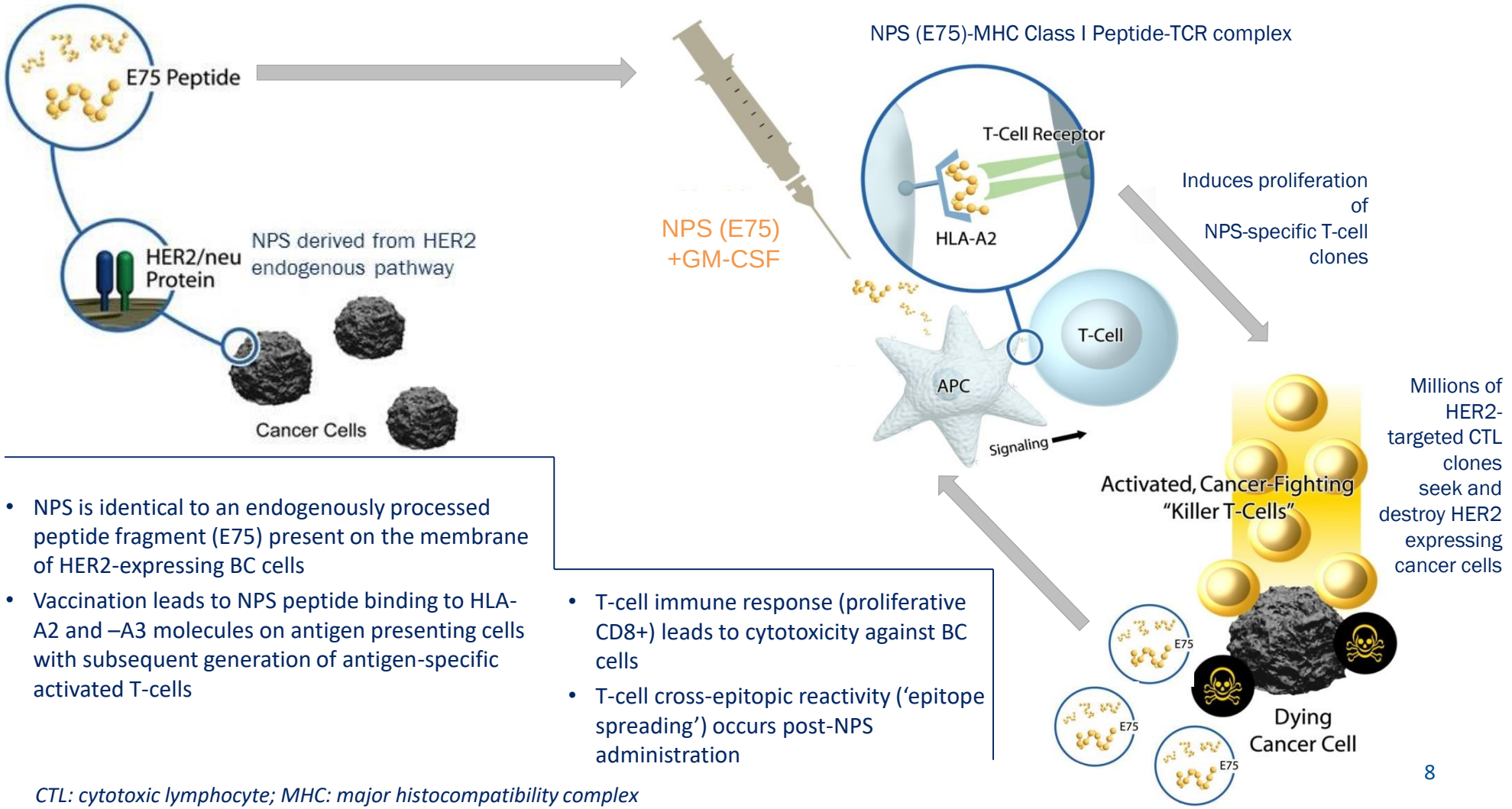
IHC Staining Data (n = 70)	MHC Class 1	
	Weak	Strong
Hercp Test 0, 1+	30	18
Hercp Test 2+, 3+	20	2
	p = 0.031	

CTLs: cytotoxic lymphocytes; ER: estrogen receptor; PgR: progesterone receptor; HercepTest: IHC quantification kit (Dako) used in the study

Inoue M, et al. Expression of MHC Class I on breast cancer cells correlates inversely with HER2 expression. Oncoimmunology. 2012;1:1104-10.

NPS MECHANISM OF ACTION: ACTIVE SPECIFIC IMMUNOTHERAPY

NPS induces de novo anti-HER2 immune response, which stimulates production of antigen-specific CD8+ cytotoxic T lymphocytes

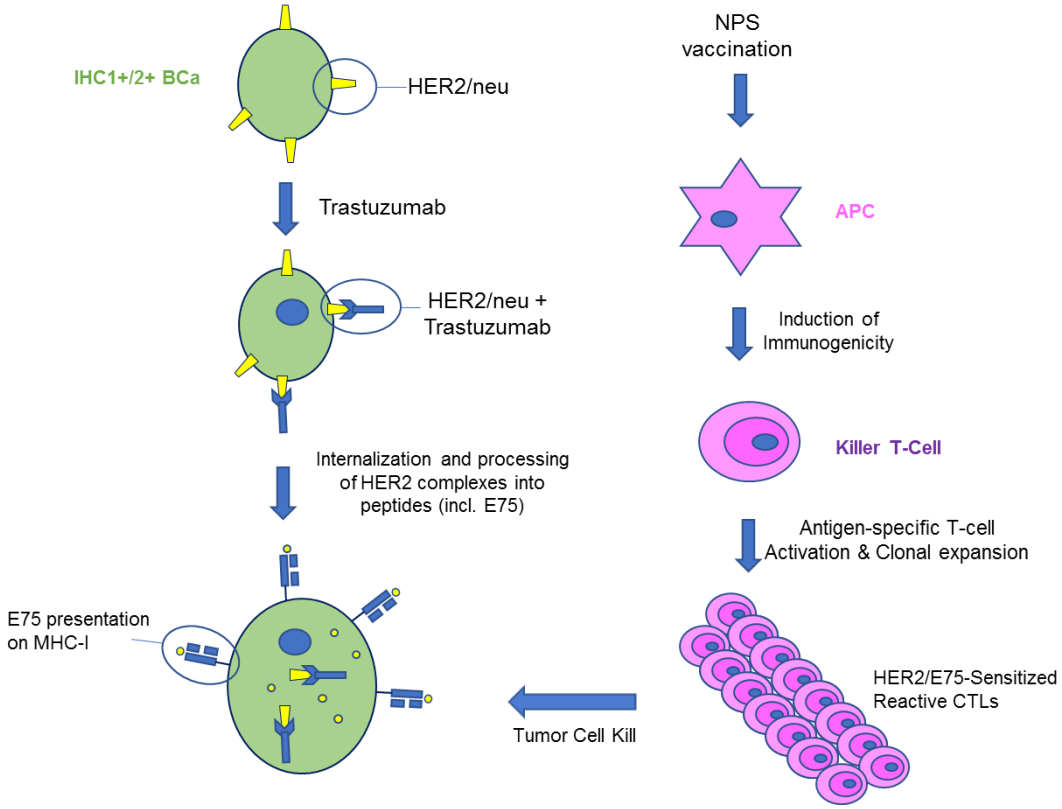


- NPS is identical to an endogenously processed peptide fragment (E75) present on the membrane of HER2-expressing BC cells
- Vaccination leads to NPS peptide binding to HLA-A2 and –A3 molecules on antigen presenting cells with subsequent generation of antigen-specific activated T-cells

- T-cell immune response (proliferative CD8+) leads to cytotoxicity against BC cells
- T-cell cross-epitopic reactivity ('epitope spreading') occurs post-NPS administration

CTL: cytotoxic lymphocyte; MHC: major histocompatibility complex

MOLECULAR/CELLULAR BASIS FOR NELIPEPIMUT-S PLUS TRASTUZUMAB SYNERGISTIC EFFECT IN HER2 IHC1+/2+ BREAST CANCER



MHC, major histocompatibility complex; PBMC, peripheral blood mononuclear cells.

Mittendorf EA, et al. Ann Surg Oncol. 2006;13:1085-98;
Gall VA, et al. Cancer Res. 2017;77:5374-83.

- Trastuzumab (TZ) is able to bind HER2 in BC cells with levels of HER2 expression lower than IHC3+
- Synergy between NPS and TZ involves significantly enhanced internalization and processing of TZ/HER2 complexes by the BC cell proteasome into short HER2 peptides (including NPS/E75) that are then presented on MHC class-I molecules (vs. in the absence of TZ)
- This significantly increased expression of vaccine target post-TZ results in enhanced immunogenicity of NPS. PBMCs from vaccinated patients efficiently recognize and lyse TZ-treated HER2-'low expressor' (IHC 1+/2+) BC cells in vitro and this effect is proportional to the dose of TZ administered.
- Subsequent release, processing and presentation of additional antigens also leads to epitope spreading
- This synergy is predictably applicable only in HER2-'low expressor' BC tumors, as HER2 IHC3+ BC cells have profoundly down-regulated MHC Class-I (mainly HLA-A) expression

NPS + TRASTUZUMAB (TZ) RANDOMIZED PHASE 2B TRIAL

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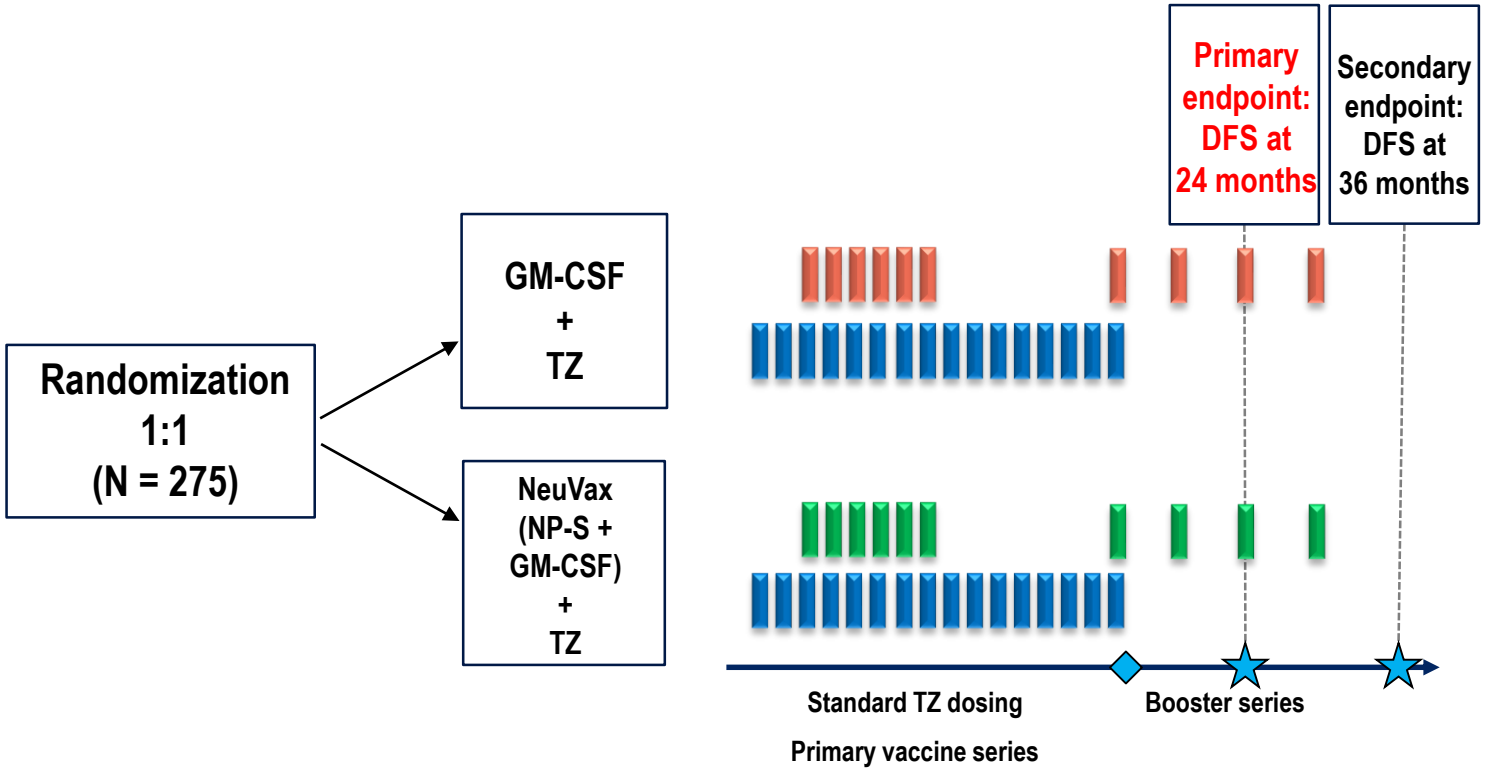
BACKGROUND

- 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.*

STUDY DESIGN



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: signal-seeking study with a priori selected cohorts and analyses**

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 AND DISEASE CHARACTERISTICS – ACTIVE VS. CONTROL

The 2 arms were well matched with regard to patient demographics and disease characteristics at the time of randomization

Patient Demographics and Baseline Disease Characteristics	NPS + Tz (n = 136)	Tz (+ GM-CSF) (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
Path (no NeoAdj) stage, n (%) I II III	 10 (16) 26 (41) 28 (44)	 9 (14) 26 (41) 28 (45)	.985

There were no significant differences between demographics in the ITT vs mITT population.

Pt Demographics & BL Diz Characteristics	NPS + Tz (n = 136)	Tz (+ GM-CSF) (n = 139)	P-Value
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

There were no significant differences between demographics in the ITT vs mITT population.

NPS: nelipepimut-S; Tz: trastuzumab; IQR: interquartile range; Path: pathological; NeoAdj: neoadjuvant (chemotherapy); ER: estrogen receptor; PR: progesterone receptor

TIMING OF ANALYSES

- **Pre-specified interim analysis (IA)** 6 months after the last patient was enrolled
- Database Lock: early MAR. 2018
- **Median follow up: 18.8 months**

MARCH 28, 2018: Independent Data Monitoring Committee strongly recommends seeking immediate regulatory guidance for further development of the NPS + Tz combination in TNBC patients

- **Final analysis (FA)** performed October 15, 2018, as planned by IDMC in March 2018.
- Database Lock: late SEP. 2018
- **Median follow up: 26.1 months**

PARAMETERS PRESENTED

- **Safety**
  - Treatment-Emergent Adverse Events (TEAE)
  - Treatment-Related Adverse even (TRAE)
- **Efficacy**
  - Median DFS along the duration of the study (log-rank/ K-M)
  - DFS rate (%) at 24 months (landmark analysis)
- <u>Populations shown</u>:
  - ITT – Entire study population
  - TNBC cohort
  - No Hormonal Rx cohort

INTERIM analysis

FINAL analysis

- **Immune Response (IR)** in vivo by Delayed Type Hypersensitivity (DTH)

TNBC COHORT PT DEMOGRAPHICS & DISEASE CHARACTERISTICS (FOR COMPARABILITY)

		Randomization Arm				
		NPS + GM-CSF + Tz N=53		Tz + GM-CSF N=45		
		N	%age	N	%age	P-value
Age	median	52.9		55.1		.469
	range	29.4-76.8		29.9-74.7		
Race	Asian	0	0.0%	2	4.4%	.452
	Black	6	11.3%	8	17.8%	
	Hispanic	4	7.5%	2	4.4%	
	Unknown	1	1.9%	1	2.2%	
	White	42	79.2%	32	71.1%	
Histology	DCIS	2	3.8%	1	2.2%	.523
	Ductal	39	73.6%	30	66.7%	
	Ductal, DCIS	8	15.1%	10	22.2%	
	Ductal, Lobular	1	1.9%	0	0.0%	
	Ductal, Lobular, DCIS	1	1.9%	0	0.0%	
	Ductal, Metaplastic	0	0.0%	2	4.4%	
	Ductal, Metaplastic, DCIS	0	0.0%	1	2.2%	
	Lobular	1	1.9%	1	2.2%	
	Metaplastic	1	1.9%	0	0.0%	
Grade	Moderate	13	24.5%	6	13.3%	.312
	Poorly	39	73.6%	37	82.2%	
	Well-Differentiated	1	1.9%	2	4.4%	
Lympho vascular Invasion		1	1.9%	0	0.0%	.651
	No	38	71.7%	33	73.3%	
	Yes	14	26.4%	12	26.7%	

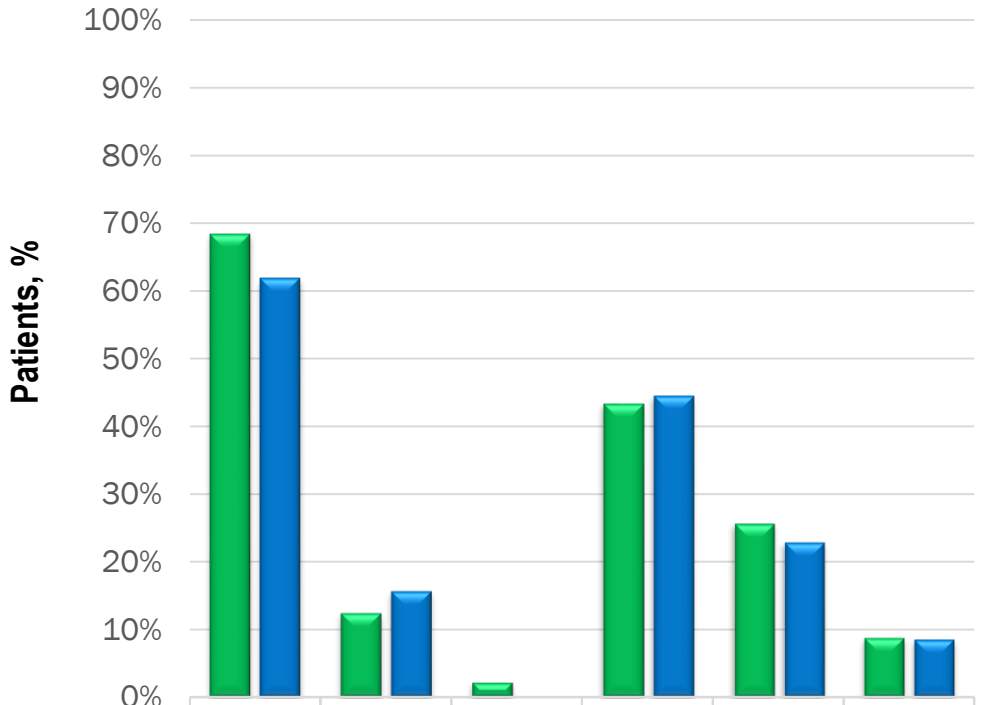
		Randomization Arm				
		NPS + GM-CSF + Tz N=53		Tz + GM-CSF N=45		
		N	%age	N	%age	P-value
AJCC7 Stage	I	10	18.9%	10	22.2%	.405
	II	27	50.9%	17	37.8%	
	III	15	28.3%	18	40.0%	
	IV	1	1.9%	0	0.0%	
Surgery	Lumpectomy	18	34.0%	15	33.3%	.751
	Lumpectomy, Mastectomy	1	1.9%	1	2.2%	
	Mastectomy	34	64.2%	28	62.2%	
	None	0	0.0%	1	2.2%	
Lymph Node Procedure	Axillary Dissection	17	32.1%	18	40.0%	.640
	SLN Bx	29	54.7%	23	51.1%	
	SLN Bx, Axillary Dissection	7	13.2%	4	8.9%	
Chemo-therapy	Adjuvant	18	34.0%	14	31.1%	.764
	Neoadjuvant	35	66.0%	31	68.9%	
XRT	Adjuvant	38	71.7%	35	77.8%	.766
	Neoadjuvant	2	3.8%	1	2.2%	
	None	13	24.5%	9	20.0%	

Active and control arms were well balanced in the TNBC cohort as well

SAFETY: TREATMENT-RELATED ADVERSE EVENTS – *FINAL* ANALYSIS

- Treatment-Emergent Adverse Events (TEAE)
  - Majority were mild or moderate (G1/2)
  - Local: 98%; systemic: 93%
  - Majority of G3 systemic TEAEs were unrelated to NPS
- Majority of Treatment-Related Adverse Events (TRAE's) were grade 1 or 2 (local injection site reactions, skin induration, pruritus, and fatigue)
- Low frequency SAEs, as expected

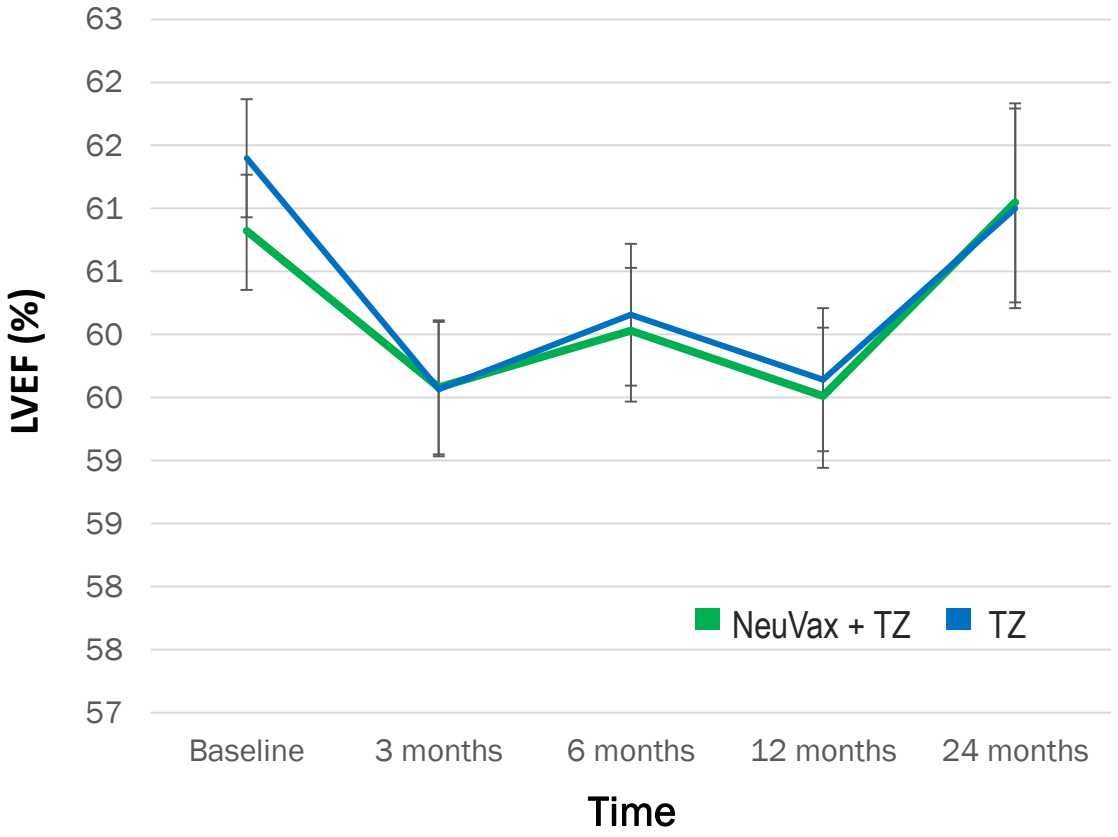
Maximum Related Graded Toxicity Per Patient



	Local (p=0.149)			Systemic (p=0.901)		
	1	2	3	1	2	3
NeuVax + TZ	68.4%	12.5%	2.2%	43.4%	25.7%	8.8%
Control + TZ	61.9%	15.8%	0.0%	44.6%	23.0%	8.6%

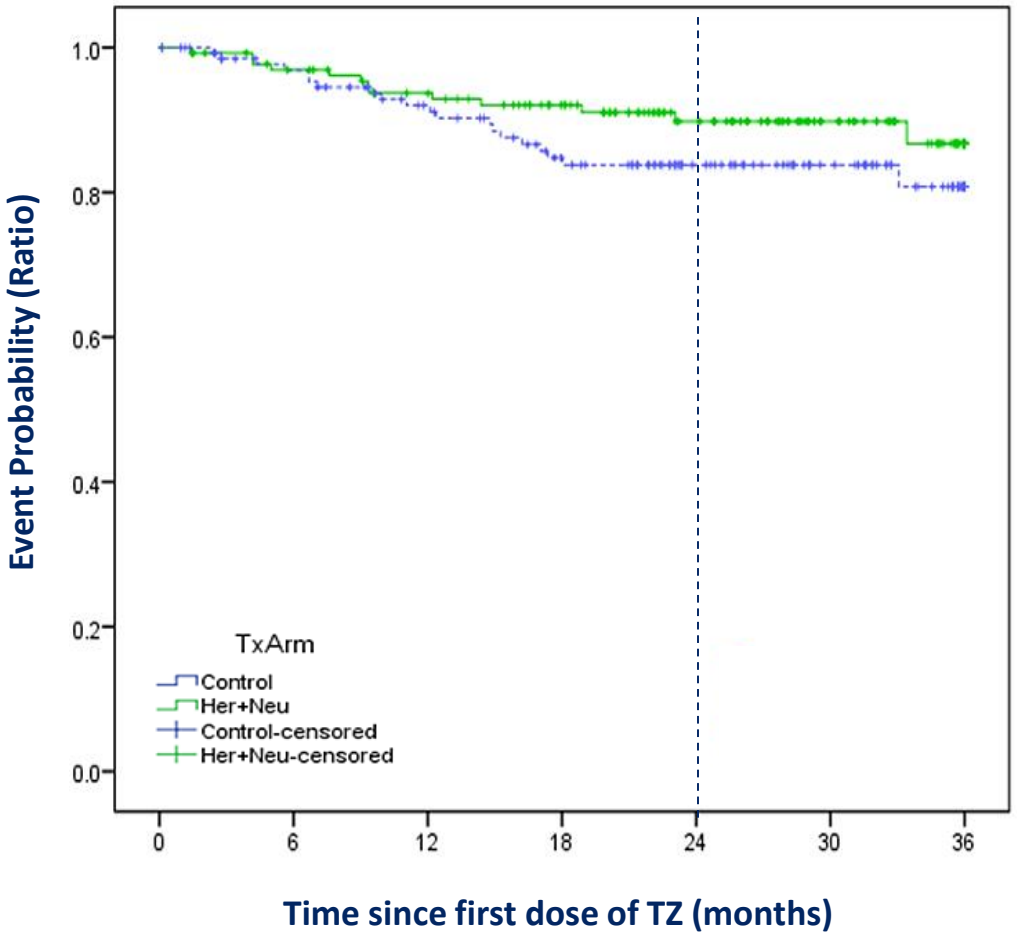
SAFETY – CARDIAC EJECTION FRACTION – *FINAL* ANALYSIS

- No difference between treatment arms in cardiac ejection fraction over time (*P* = .558) and at each time point
- The addition of NeuVax to TZ did not result in any additional cardiotoxicity compared with TZ alone



LVEF: Left Ventricular Ejection Fraction
TZ: trastuzumab

ITT POPULATION - DISEASE FREE SURVIVAL (DFS) – *FINAL* ANALYSIS



ITT POPULATION

P = .175

HR = 0.62 (across the duration of the study)

37.0% reduction in risk of recurrence or death at 24 mo.

Control

N = 139

Median F/U = 25.7 mo.

24-mo DFS = 83.8%

Active

N = 136

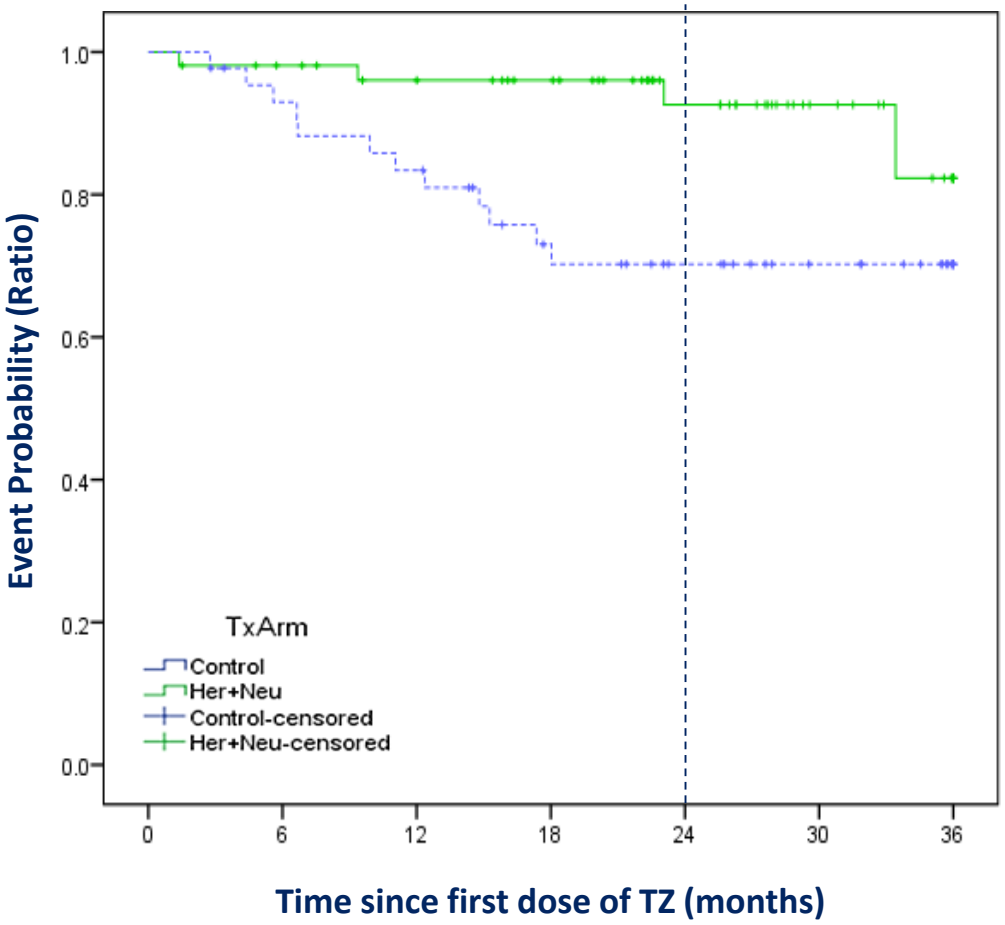
Median F/U = 25.7 mo.

24-mo DFS = 89.8%

Interim Analysis:
P = .257
HR = 0.67
Med. F/U = 19.6 mo
34.9% reduction in risk

Trending toward a difference in median DFS in favor of the combination arm

TNBC COHORT - 97 PATIENTS (36% OF ITT) - DISEASE FREE SURVIVAL – *FINAL* ANALYSIS



TNBC COHORT (36% of ITT)

P = .013

HR = 0.260

75.2% reduction in risk of recurrence or death at 24 mo.

Control

N=44

Median F/U = 26.1 mo.

24 mo. DFS = 70.2%

Active

N=53

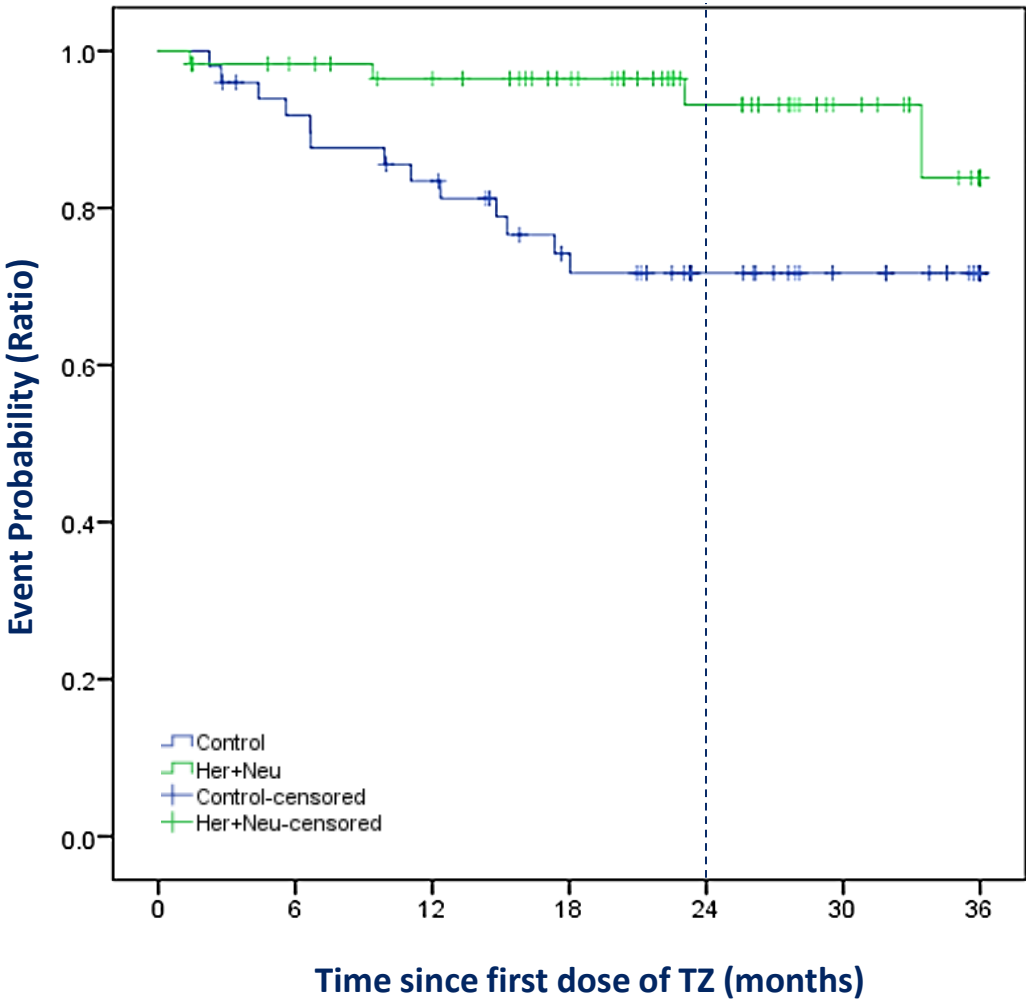
Median F/U = 26.1 mo.

24 mo. DFS = 92.6%

Interim Analysis:
P = .023
HR = 0.26
Med. F/U = 19.3 mo
70.4% reduction in risk

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

NO HORMONE TREATMENT COHORT – 110 PATIENTS (40% OF ITT) - DISEASE FREE SURVIVAL *FINAL* ANALYSIS



Includes only patients that did not receive hormonal therapy: approx. overlapping with TNBC subgroup (40% of the total study population)

NO HORMONE TREATMENT COHORT

P = .008

HR = 0.246

75.9% reduction in risk of recurrence or death at 24 mo.

Control

N=50

Median F/U = 25.6 months

24-mo DFS = 71.7%

Active

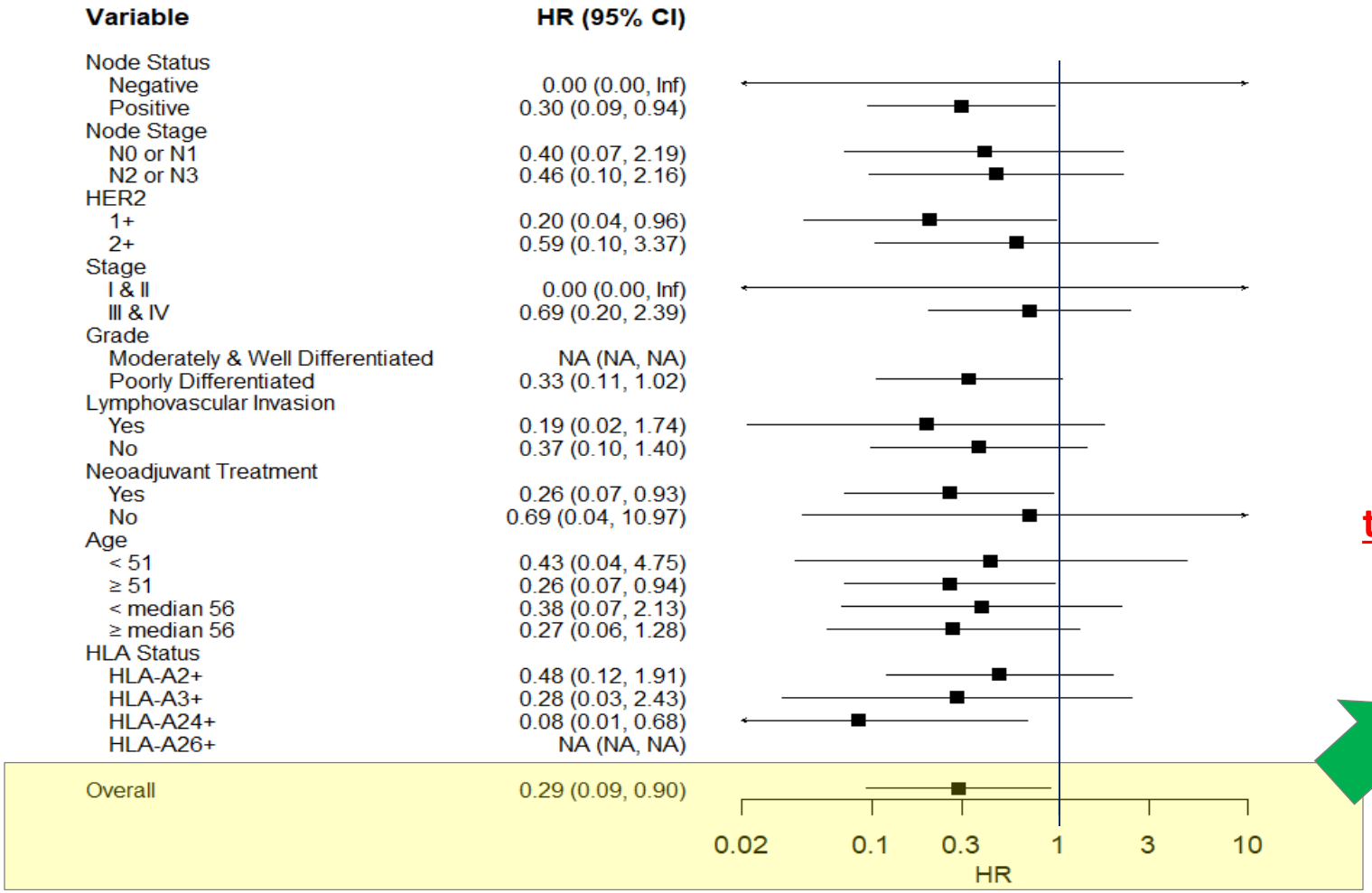
N=60

Median F/U = 25.6 months

24-mo DFS = 93.2%

Interim Analysis:
P = .009
HR = 0.238
Med. F/U = 18.5 mo
73.4% reduction in risk

FOREST PLOT FOR VARIOUS COHORTS BASED ON DICHOTOMOUS DATA CUTS FOR EACH VARIABLE TESTED (LOG HR SCALE) – TNBC COHORT – *INTERIM* ANALYSIS

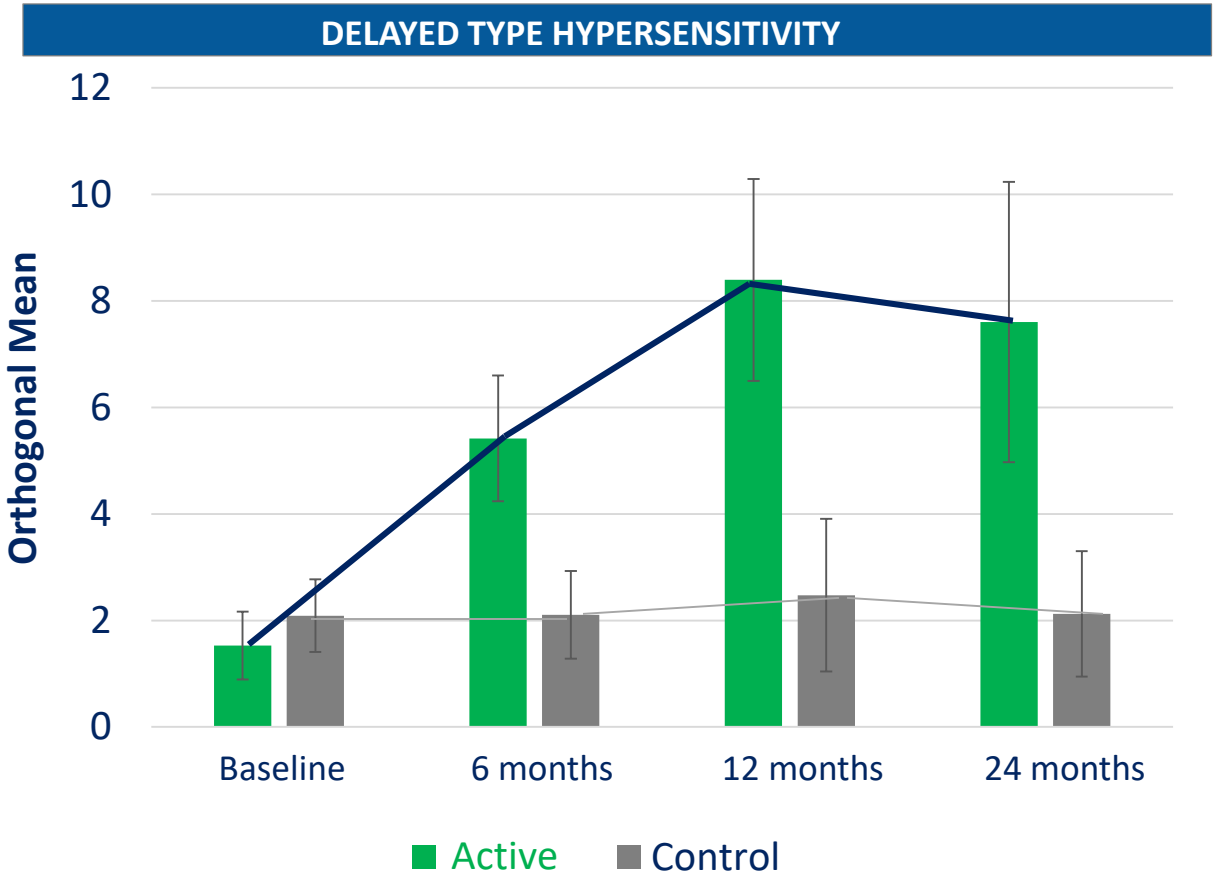


Relative <u>decrease</u> in the risk of progression or death <u>over</u> the study time <u>period</u> of 71%

TNBC cohort: difference between the active and control arm persists across a wide set of patient and disease variables, including HLA allele type

IN VIVO IMMUNE RESPONSE (IR) BY DELAYED TYPE HYPERSENSITIVITY (DTH)

- There was a statistically significant difference between IR (by DTH) between the Control and Active (NPS) arms
  - Over time across all time points: P = .002
- Within the Control arm, there was no difference among IR readouts over time (P = .896)
- Within the Active (NPS) arm, there was a significant increase in IR readouts over time (P = .000023)



Note: time points represent 6 month intervals from baseline.

CONCLUSIONS

- Treatment-emergent AE's were of mild or moderate severity
  - No enhanced cardiac toxicity with the combination vs. TZ alone
- NPS + TZ may provide clinically meaningful benefit to patients with HER2 low-expressing breast cancers
- The NPS + TZ combination in the adjuvant setting demonstrated clinically meaningful and statistically significant improvement in DFS in patients with early-stage TNBC
- SELLAS is actively seeking regulatory input by the FDA and EMA
- Global Clinical and Regulatory Key Opinion Leaders supportive of strategy to pursue expeditious development of NPS for TNBC patients for which there is a great unmet medical need

THANK YOU!

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