

BACKGROUND

Her2 low-expressing (LE) (IHC 1-2+, FISH non-amplified) breast cancer (BC) patients (pts) have not benefited from HER2-directed therapy, despite HER2 antigen availability. Specifically, triple negative BC (TNBC) is immunogenic and in need of additional therapeutic options. Our group has previously shown HER2-derived nelipeptimut-S (NPS; E75) + GM-CSF (NeuVax) to be synergistic with trastuzumab (Tz) in pre-clinical and pilot clinical studies. In an interim analysis of a multicenter, prospective, randomized, single-blinded, placebo-controlled phase 2b trial of Tz + NeuVax vs Tz to reduce recurrence in HER2 LE, node positive (NP) and/or TNBC pts, we previously reported that the combination Rx was safe (without added cardiac toxicity) and demonstrated a clinically meaningful and stat. significant prolongation in disease-free survival (DFS) in TNBC pts. This analysis examines additional subsets in this trial and assesses patterns of recurrence in the TNBC cohort.

METHODS

- HER2 LE, NP, and/or TNBC pts who were clinically disease-free after standard therapy were randomized to receive either Tz+NeuVax (vaccine group; VG) or Tz+GM-CSF (control group; CG)
- Nelipeptimut-S (NPS; E75; HER2 369-377; KIFGLSAFL) is a 9-amino peptide produced by solid-phase peptide synthesis
- All pts received 1 year Tz therapy; NeuVax or GM-CSF treatment occurred every 3 weeks x 6 starting with 3rd Tz dose; boosters given every 6 months x 4
- Primary endpoint: intention-to-treat 24 month disease-free survival (DFS) evaluated by log rank
- Only patients with TNBC were included in this subgroup analysis and assessment of patterns of relapse.
- Stage determined by clinical stage if patient received neoadjuvant chemotherapy and pathologic stage if patient did not receive neoadjuvant chemotherapy

RESULTS

- 97 pts w/ TNBC included in subgroup analysis; VG = 53, CG = 44
- No significant clinicopathologic differences between groups (Table)
- DFS higher overall in VG vs CG group (82.3% vs 70.2%); p=0.013; hazard ratio (HR) .262, 95% confidence interval (CI) .084-.814 (Fig. 1); on TNBC subgroup analysis, DFS was higher in VG vs CG among patients who received neoadjuvant chemotherapy (p=0.013; HR .226, CI .063-.815, Fig. 2), had HER2 IHC 1+ BC (p=0.014; HR .178, CI .038-.837, Fig. 3), were ≥51 years of age (p=0.004; HR .144, CI .031-.656, Fig. 4), or were AJCC 7th edition stage I/II (p=0.006; HR incalculable, Fig. 5)
- VG pts had a lower rate of local-regional disease as the site of the first clinically detected recurrence (p=0.004 across all sites; p=0.01 for locoregional relapses, Fig. 6)

		Vaccine Group (n=53)	Control Group (n=44)	p value
Age (median)		52.9	55.5	0.47
	IQR	29.4-76.8	29.9-74.7	
Race	White	42 (79.2%)	31 (70.4%)	0.74
	Asian	0 (0.0%)	2 (4.5%)	
	Black	6 (11.3%)	8 (18.2%)	
	Hispanic	4 (7.5%)	2 (4.5%)	
	Unknown	1 (1.8%)	1 (2.3%)	
Nottingham modified, Scarff-Bloom-Richardson Grade	Grade 1	1 (1.9%)	2 (4.5%)	0.33
	Grade 2	13 (24.5%)	6 (13.6%)	
	Grade 3	39 (73.6%)	36 (81.8%)	
HER2 IHC	HER2 1+	34 (64.1%)	27 (61.3%)	0.78
	HER2 2+	19 (35.8%)	17 (38.6%)	
Chemotherapy	Neoadjuvant	35 (66.0%)	30 (68.2%)	0.82
	Adjuvant	18 (34.0%)	14 (31.8%)	
Radiation	Adjuvant	40 (75.5%)	35 (79.5%)	0.63
	None	13 (24.5%)	9 (20.5%)	
Breast Surgery	BCT	18 (34.0%)	15 (34.1%)	0.93
	Mastectomy	35 (66.0%)	27 (61.4%)	
	None	0 (0.0%)	1 (2.3%)	
Axillary Surgery	Ax. Dissection	29 (54.7%)	23 (52.3%)	0.81
	SLN biopsy	24 (45.3%)	21 (47.7%)	
AJCC Stage	I	10 (18.9%)	10 (22.7%)	0.48
	II	27 (50.9%)	17 (38.7%)	
	III	15 (28.3%)	16 (36.3%)	
	IV	1 (1.8%)	0 (0.0%)	

Table: Demographics

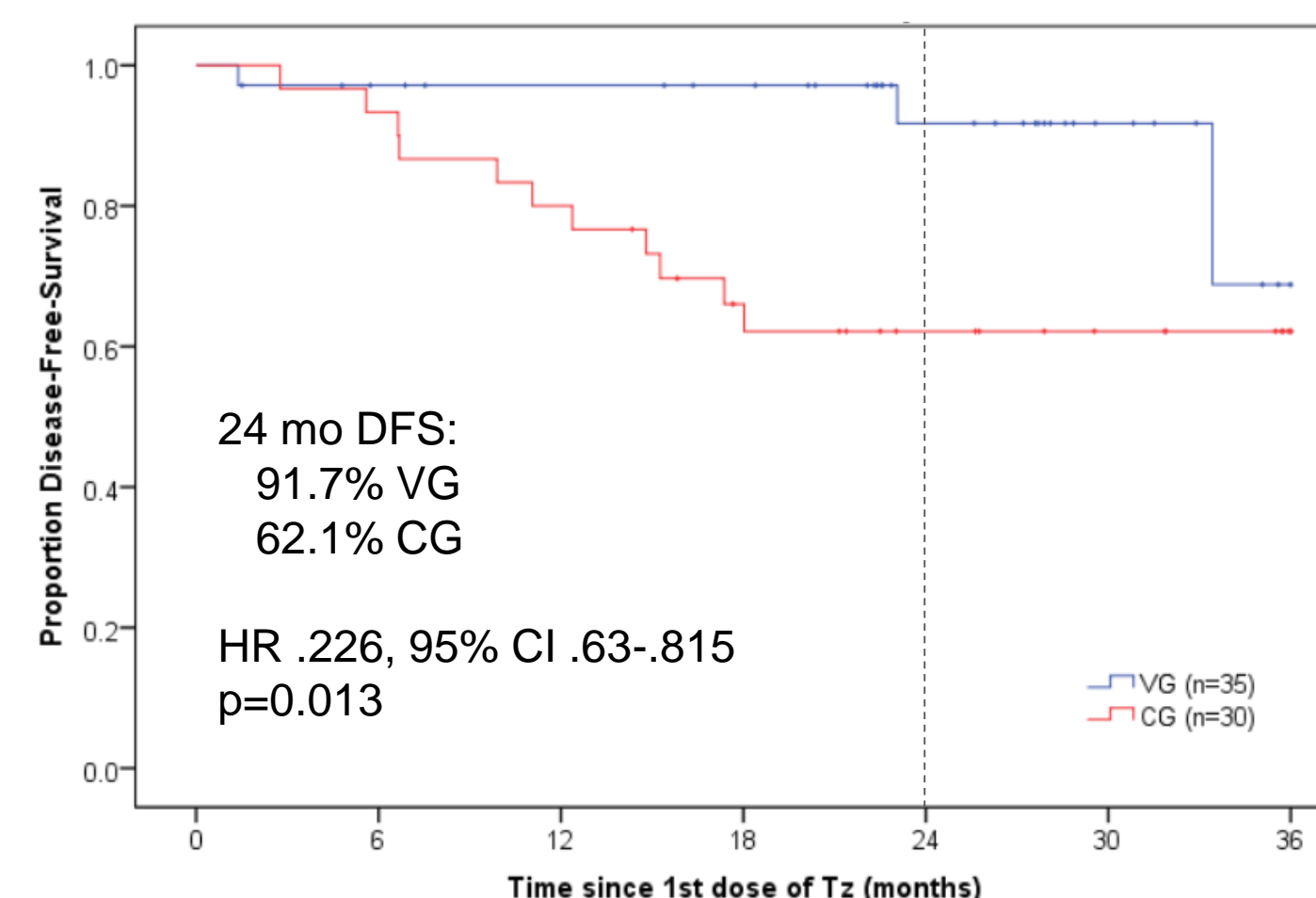


Fig. 2: Received neoadjuvant chemotherapy

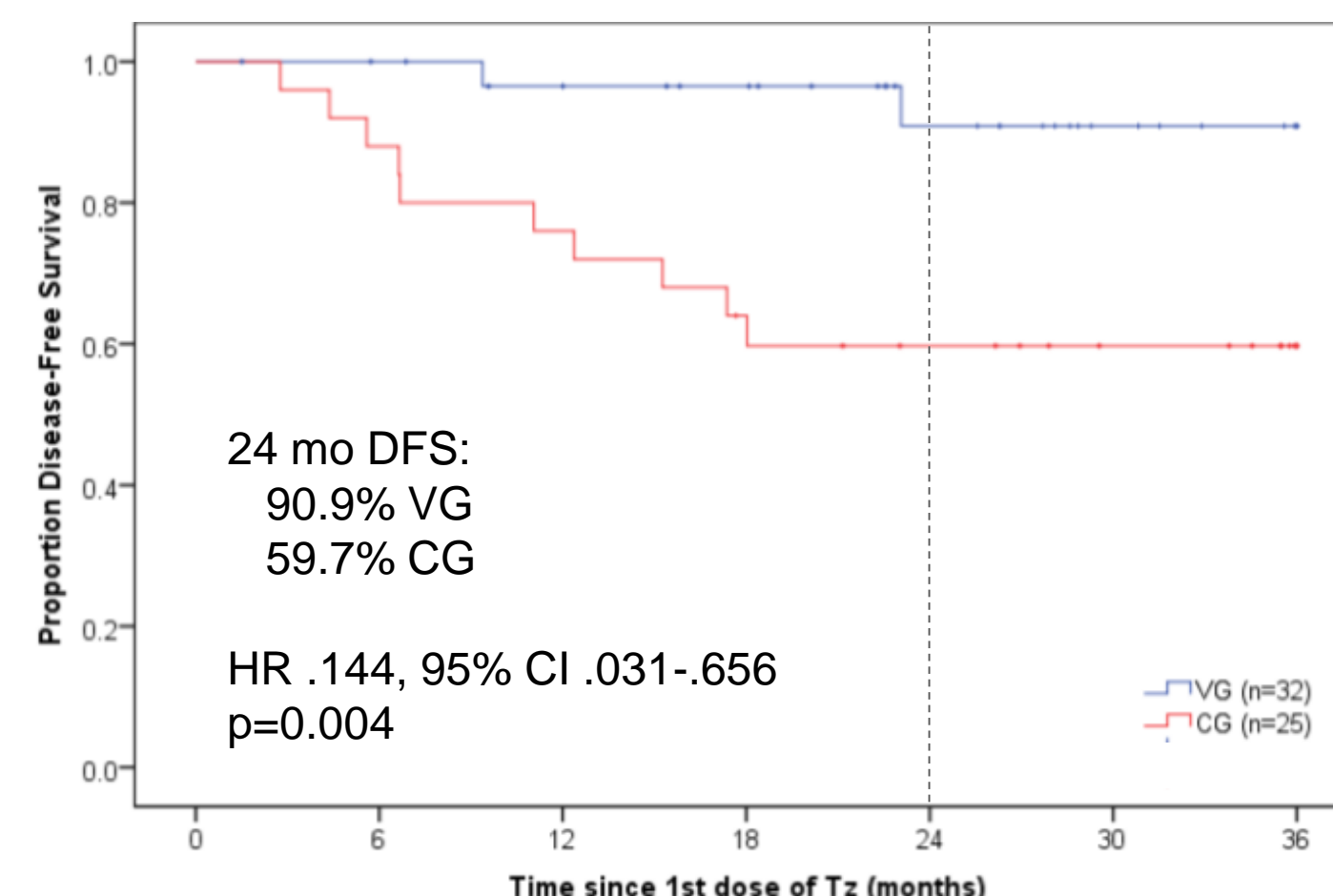


Fig. 4: Patients ≥51 years of age

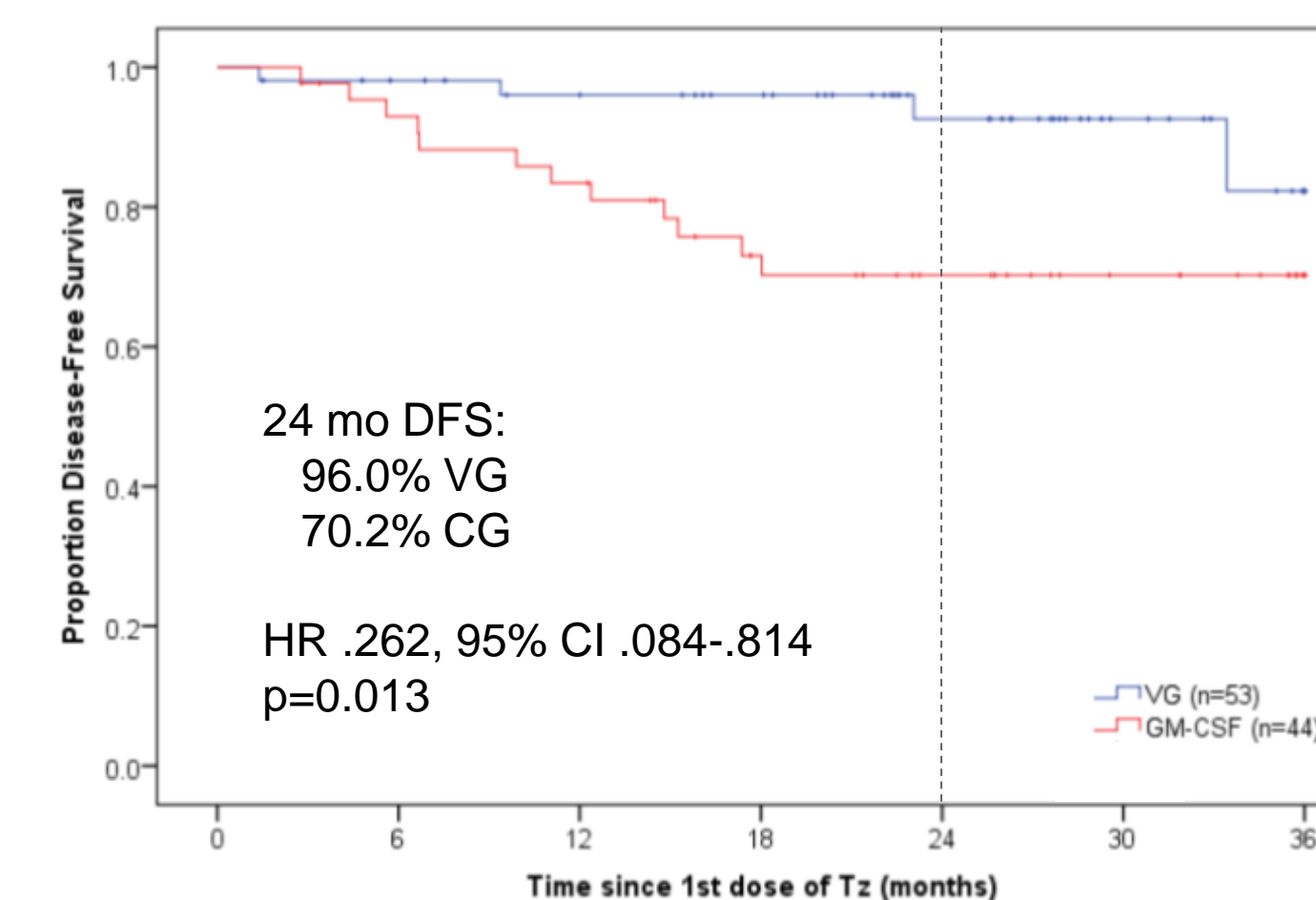


Fig. 1: All patients (Intention to treat)

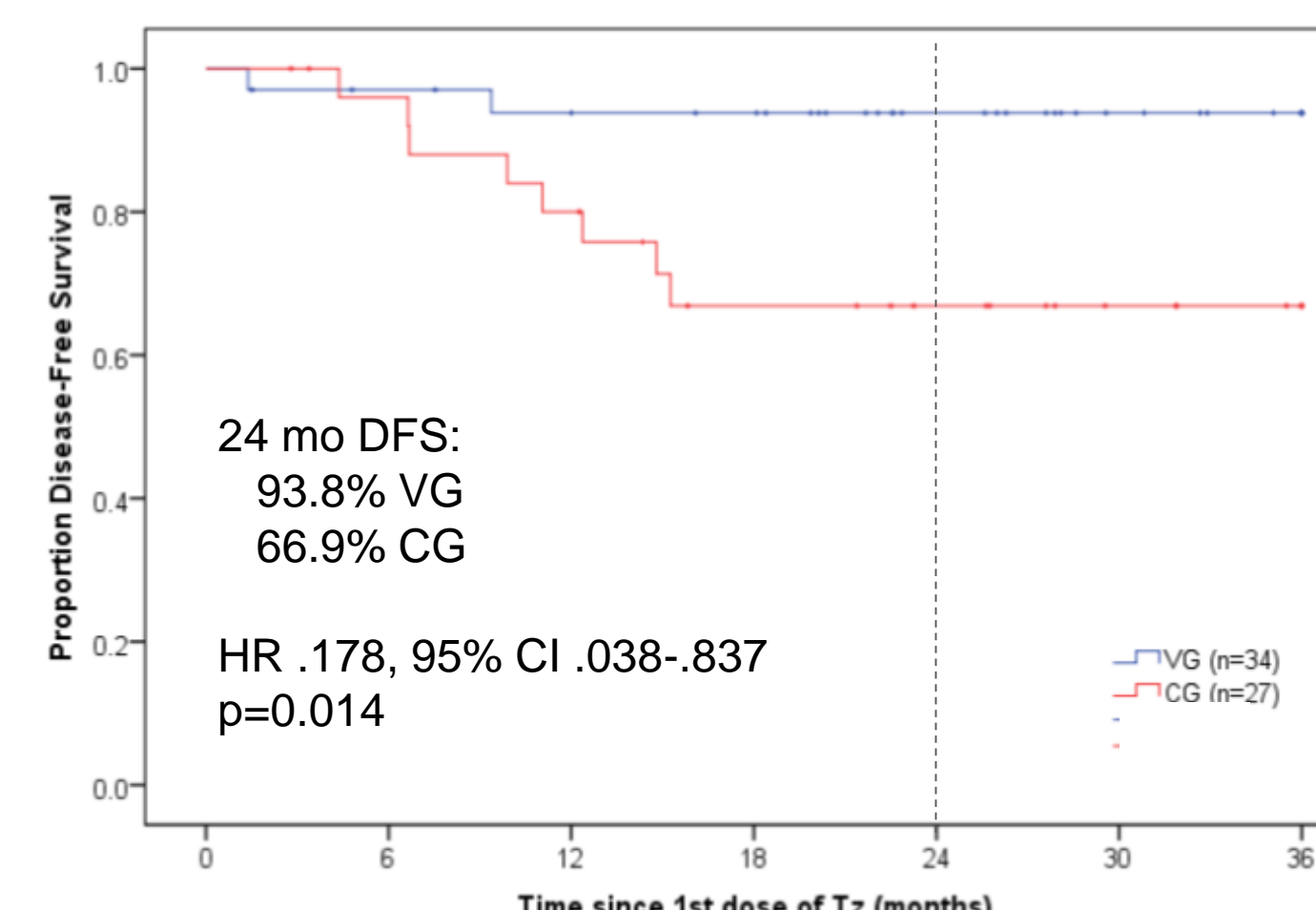


Fig. 3: Patients with HER2 IHC 1+ BC

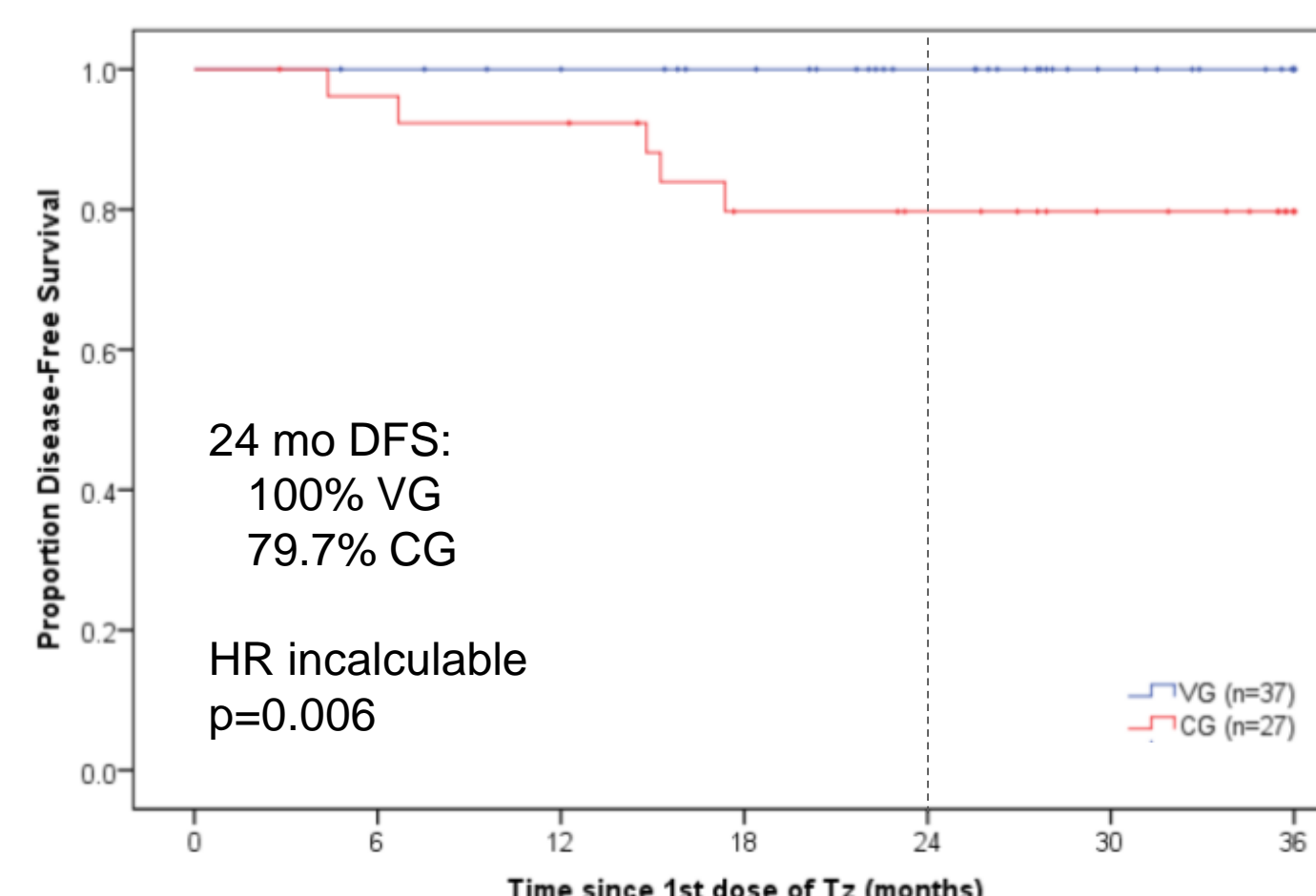


Fig. 5: Patients with stage I/II BC

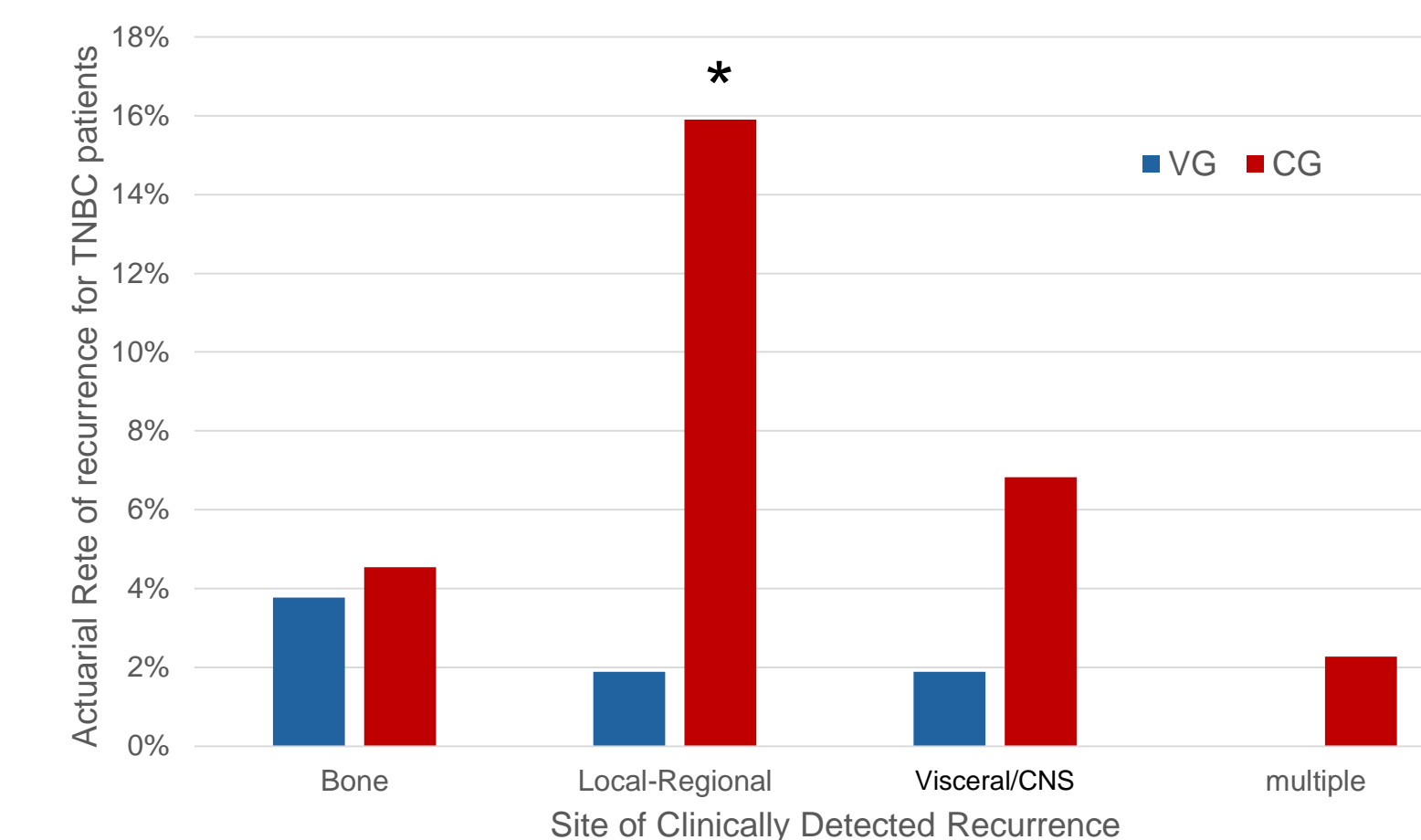


Fig. 6: Site of clinically detected recurrence. p=0.004 across all relapse sites; * p=0.01 for locoregional relapses

CONCLUSIONS

- Patients with TNBC in the VG received a significant clinical benefit
- Within the TNBC cohort, specific benefit was seen in patients who received neoadjuvant chemotherapy, expressed lower HER2, were 51 years or older, or had AJCC 7th edition stage I/II TNBC
- Relapse rates were significantly lower in the VG group across sites, as well as specifically for locoregional relapses
- These factors may help enrich the TNBC population targeted in a definitive phase 3 study in TNBC with residual disease after neoadjuvant chemotherapy

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 nelipeptimut-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
- The study was sponsored by Cancer Insight, LLC, and was supported by SELLAS Life Sciences Group, Inc.