HERIZON: A Phase 2 study of HER-Vaxx (IMU-131), a HER2 targeting peptide vaccine, plus standard of care chemotherapy in patients with HER2 overexpressing metastatic or advanced gastric/GEJ adenocarcinoma. Final Overall Survival Analysis

Marina Maglakelidze[1], Dinara Ryspayeva[2], Zoran Andric[3], Zoran Petrovic[4], Iurie Bulat[5], Ivan Nikolic[6], Rajnish Nagarkar[7], Ursula Wiedermann[8], Brent Blumenstein[9], Leslie Mi Ok Chong[10], Nicholas J. Ede[10], Bonnie Nixon[10], Sharon Yavrom[10], Giovanni Selvaggi[10], Anthony J. Good[10], Tanuj Chawla[11]

[1]ARENSIA Exploratory Medicine LLC, Tbilisi, Georgia; [2]ARENSIA Exploratory Medicine LLC, Kyiv, Ukraine; [3]Clinical Hospital Center Bezanijska Kosa, Belgrade, Serbia; [4]Military Medical Academy, Belgrade, Serbia; [5]ARENSIA Exploratory Medicine Research Unit, Institute of Oncology, Chisinau, Republic of Moldova; [6]Oncology Institute of Vojvodina, Sremska Kamenica, Serbia ; [7]HCG Manavata Cancer Centre, Nashik, India ; [8]Medical University, Vienna, Austria ; [9]Trial Architecture Consulting, Maryland, USA ; [10]Imugene Limited, Sydney, Australia ; [11]Tata Medical Centre, Kolkata, India

Tanuj Chawla, MD

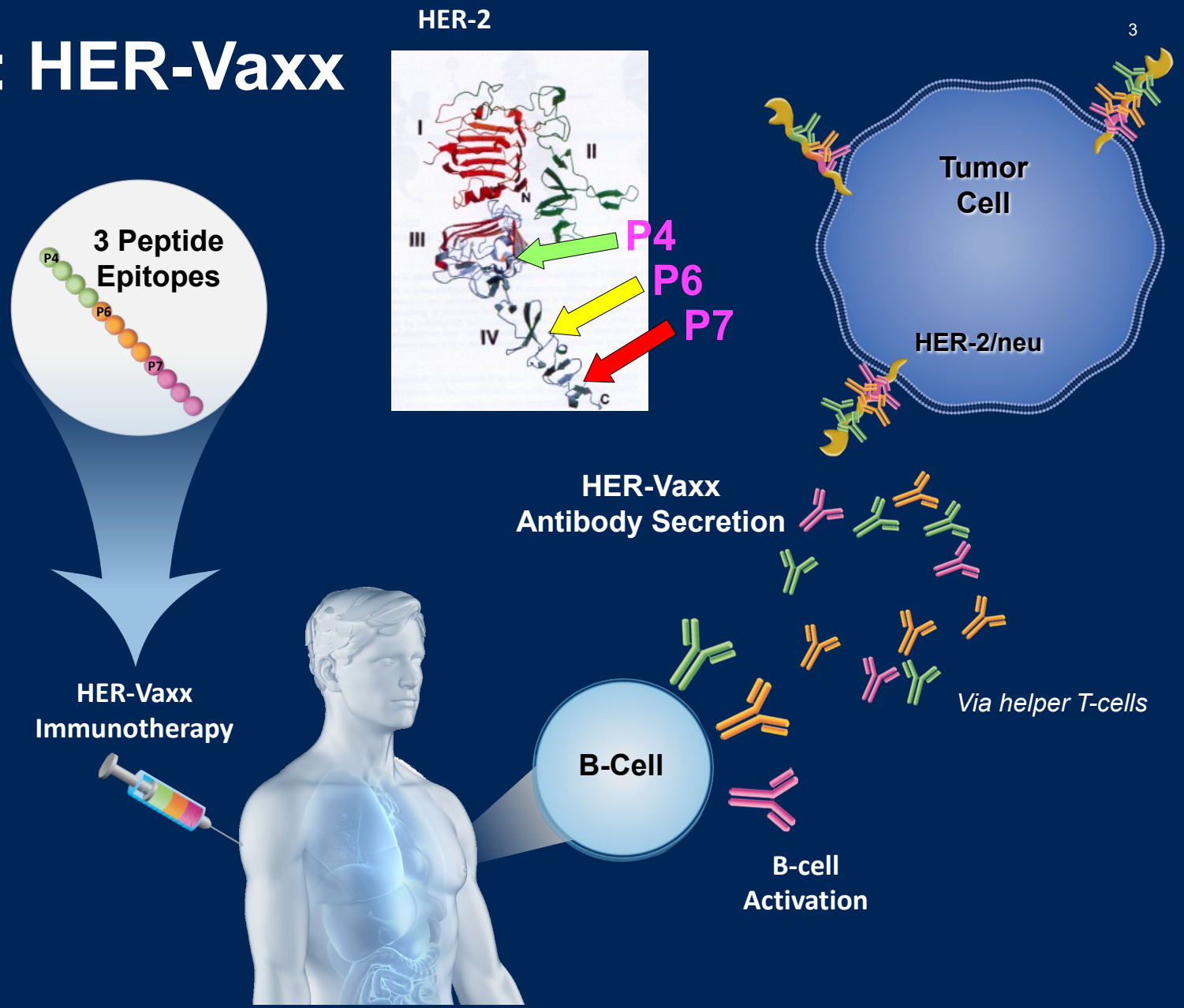
Kolkata, India

DECLARATION OF INTERESTS

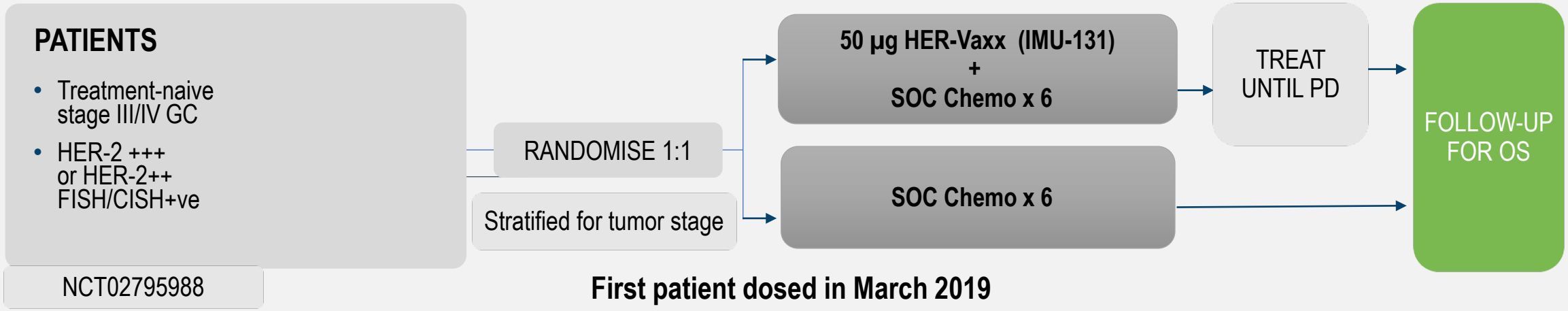
- Study related funds provided to my institution by the study sponsor, Imugene Limited.
- Travel grant to attend ASCO GI 2023, provided by Imugene Limited.

B Cell Immunotherapy: HER-Vaxx

- HER-Vaxx is a B cell Immunotherapy designed to treat tumours that over-express the HER-2/neu receptor, including gastric
- HER-Vaxx is constructed from three B-cell epitopes (P4, P6, P7) derived from the extracellular domain of HER-2/neu
- The 3 peptide epitopes are conjugated to carrier protein CRM197 in a Montanide Th1 (adjuvant) emulsion
- HER-Vaxx has been shown in pre-clinical studies and in the Phase Ib study to stimulate a potent polyclonal antibody response to HER2/neu
- HERIZON study was designed and conducted in countries where trastuzumab was not available to replicate the pivotal trastuzumab/ chemotherapy study (TOGA) in gastric cancer.



HERIZON Phase 2 Open Label, Multicenter Study



First patient dosed in March 2019

HER-Vaxx I.M.	C1D1, C1D15, C2D15 and C4D15 then Q9 weeks till PD
Chemotherapy	6 cycles Q3 weeks (Cisplatin + 5FU or Capecitabine; Oxaliplatin + Capecitabine)

PRIMARY ENDPOINT	**OS** (pre-spec 1-sided alpha 0.10, power 90% with critical HR 0.6 and 24 events)
SECONDARY ENDPOINTS	PFS, Safety, Immune Response

NO. OF PATIENTS	36
SITE LOCATION	Eastern Europe, India

Baseline Demographics and Characteristics

	HER-Vaxx + Chemotherapy N=19 (%)	Chemotherapy N=17 (%)
Median Age [years] (range)	65 (48, 84)	68 (44, 79)
M/F	10 (53)/9 (47)	13 (77)/4 (23)
ECOG performance grade, n (%)		
Grade 0	8 (42)	8 (47)
Grade 1/2	11 (58)	9 (53)
Initial tumor diagnosis type, n (%)		
Adenocarcinoma of gastroesophageal junction	2 (10)	2 (12)
Adenocarcinoma of the stomach	17 (90)	15 (88)
Tumor stage at screening, n (%)		
Stage IIIb	5 (26)	4 (24)
Stage V	14 (74)	13 (77)
Prior treatment n (%)		
Prior gastric cancer surgery	10 (53)	7 (41)
Prior gastric cancer drug therapy	4 (21)	2 (12)
Prior gastric cancer radiotherapy	1 (5)	0

5 patients

Data cut 01Jun22

No Additive Toxicity to Chemotherapy with HER-Vaxx

Safety Overview

	HER-Vaxx + Chemotherapy N=19 (%)	Chemotherapy N=17 (%)
Any TEAE	18 (95)	16 (94)
Any serious TEAE	2 (11)	5 (29)
≥ Grade 3	8 (42)	7 (42)
Treatment-related TEAE	16 (84)	13 (77)
TEAE leading to treatment discontinuation	2 (11)	4 (24)
TEAE leading to treatment reduction or interruption	8 (42)	6 (35)
Any TEAE leading to death	1 (5)	1 (6)

One patient in each arm experienced a Grade 5 event:

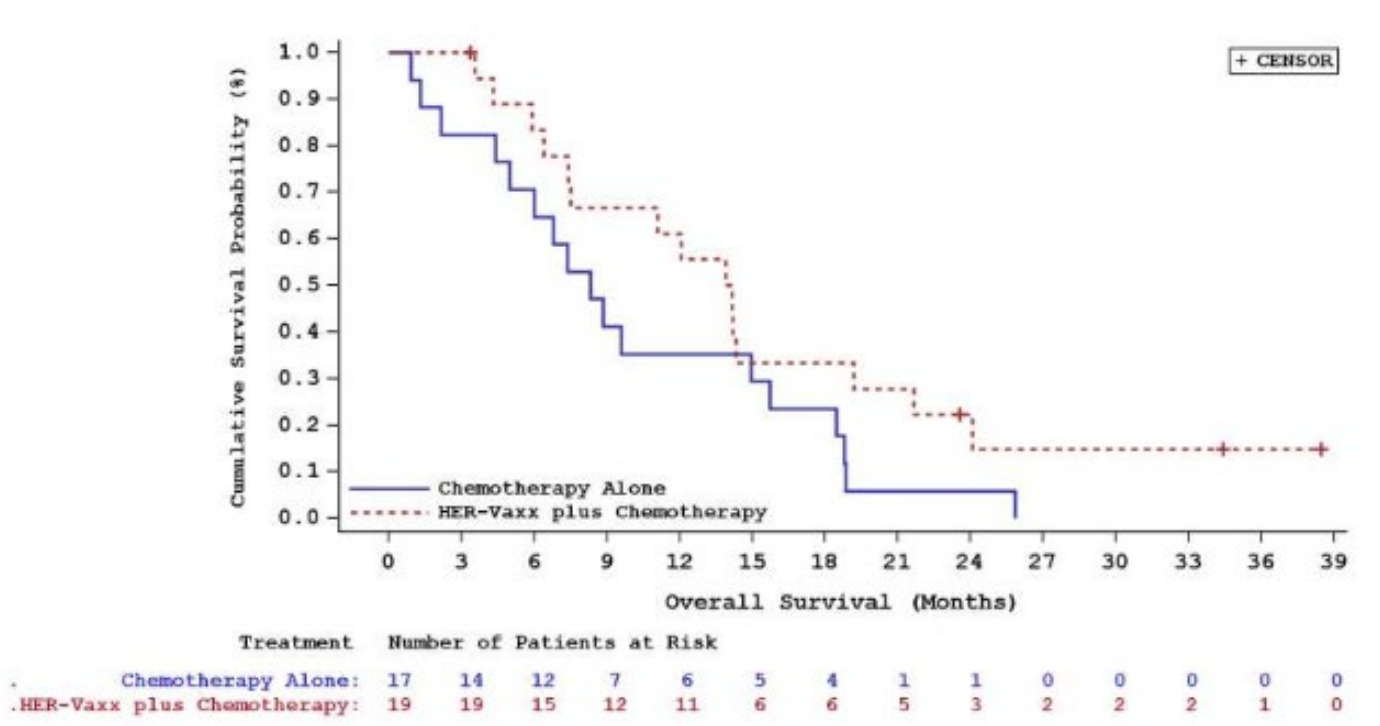
- Grade 5 Covid infection in the HER-Vaxx + chemotherapy arm
- Grade 5 respiratory failure in the chemotherapy alone arm

Adverse Event in ≥ 10% of Patients

	HER-Vaxx + Chemotherapy N=19 (%)		Chemotherapy N=17 (%)	
	Grade 1/2	Grade ≥ 3	Grade 1/2	Grade ≥ 3
Decreased appetite	5 (26)	0	1 (6)	0
Headache	5 (26)	0	0	0
Diarrhoea	4 (21)	1 (5)	3 (18)	0
Nausea	4 (21)	0	1 (6)	0
Fatigue	3 (16)	2 (11)	2 (12)	0
Vomiting	3 (16)	0	3 (18)	0
Anaemia	2 (11)	1 (5)	1 (6)	4 (24)
Injection site reaction	2 (11)	0	0	0
Pain in extremities	2 (11)	0	0	0
Peripheral swelling	2 (11)	0	0	0
Weight decreased	2 (11)	0	1 (6)	0
Platelet count decreased	0	1 (5)	3 (18)	1 (6)
Hypoalbuminemia	0	0	2 (12)	0
Peripheral neuropathy	0	0	2 (12)	0

Data cut 01Jun22

Overall Survival Benefit when is HER-Vaxx Added to Chemotherapy



Six patients/arm received post-treatment therapy including 5 patients who recieved trastuzumab (3 in the HER-Vaxx arm and 2 in chemotherapy arm).

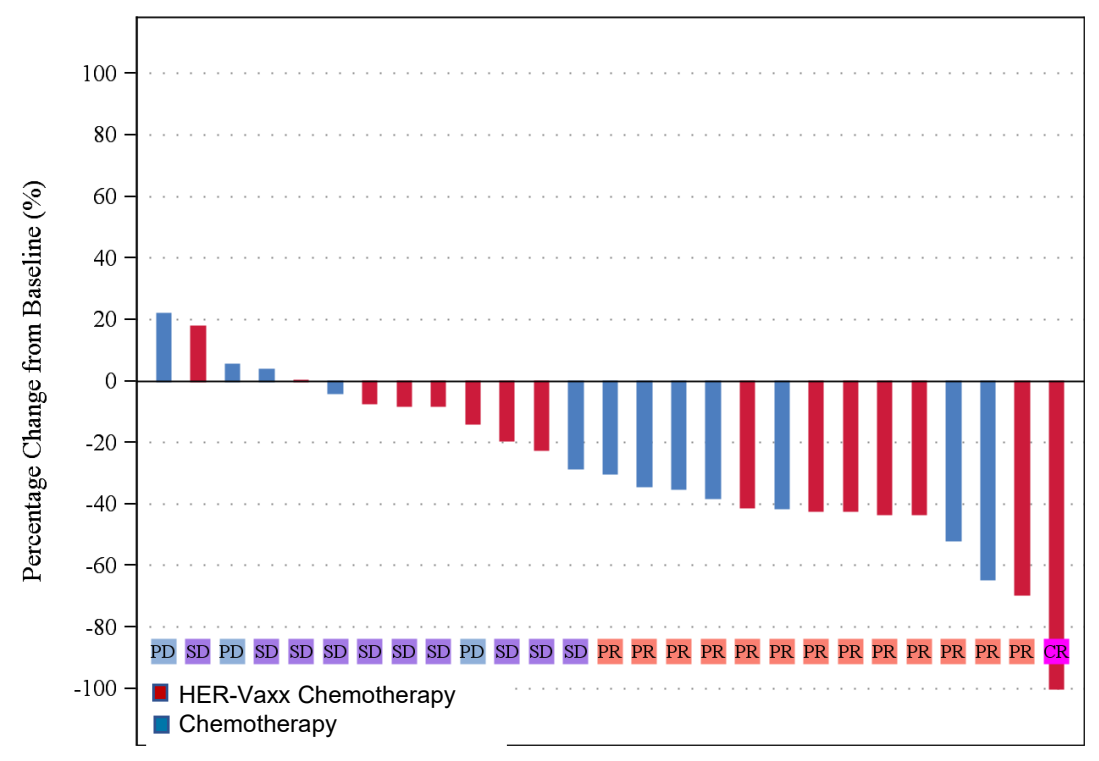
	HER-Vaxx + Chemotherapy	Chemotherapy
Sample Size	19	17
Events	15	17
Median OS (2-sided 80% CI)	**14.0 months (11.1, 14.3)**	8.3 months (6.0, 9.59
HR	**0.558**	
2-sided 80%CI	(0.349, 0.895)	
Log-rank Test (1-sided p-value)	**0.054***	
Median PFS (2-sided 80% CI)	6.93 (5.6, 9.9)	6.01 (2.2, 8.3)

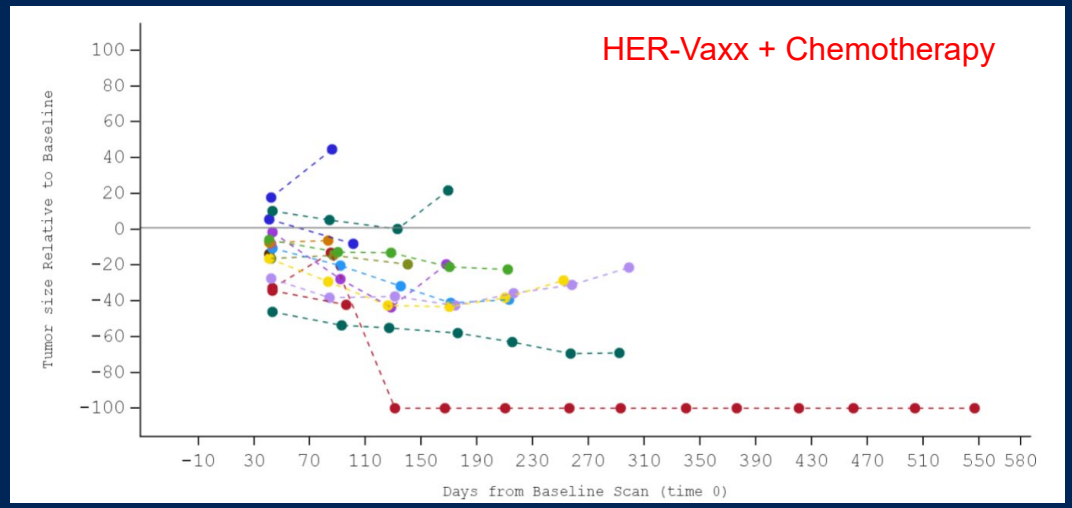
*Significant, 1-sided $p < 0.10$

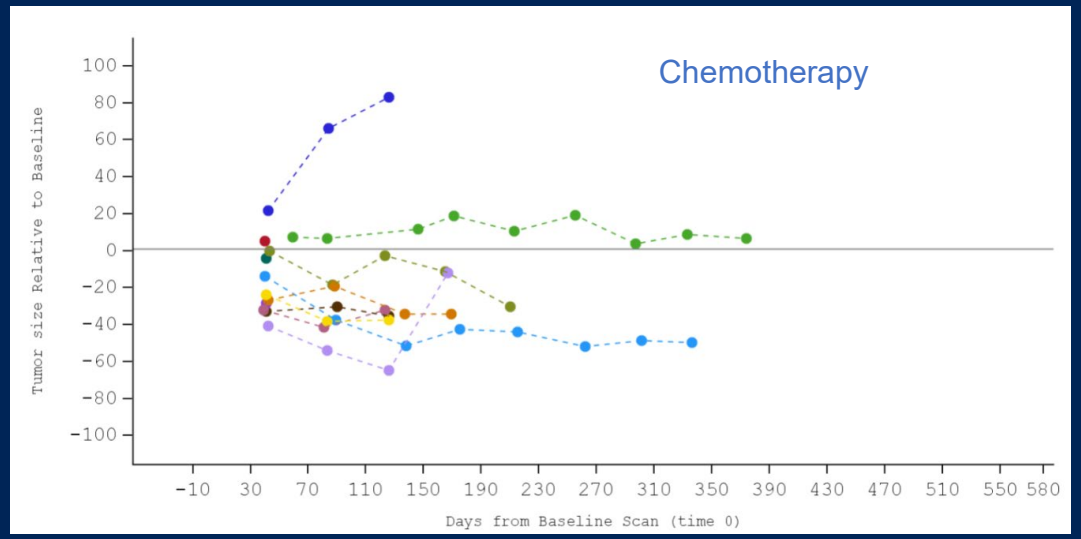
Data cut 01Jun22 Data Extract Date: 26DEC2022

HER-Vaxx added to Chemotherapy Demonstrated Deep and Durable Responses

Best overall response



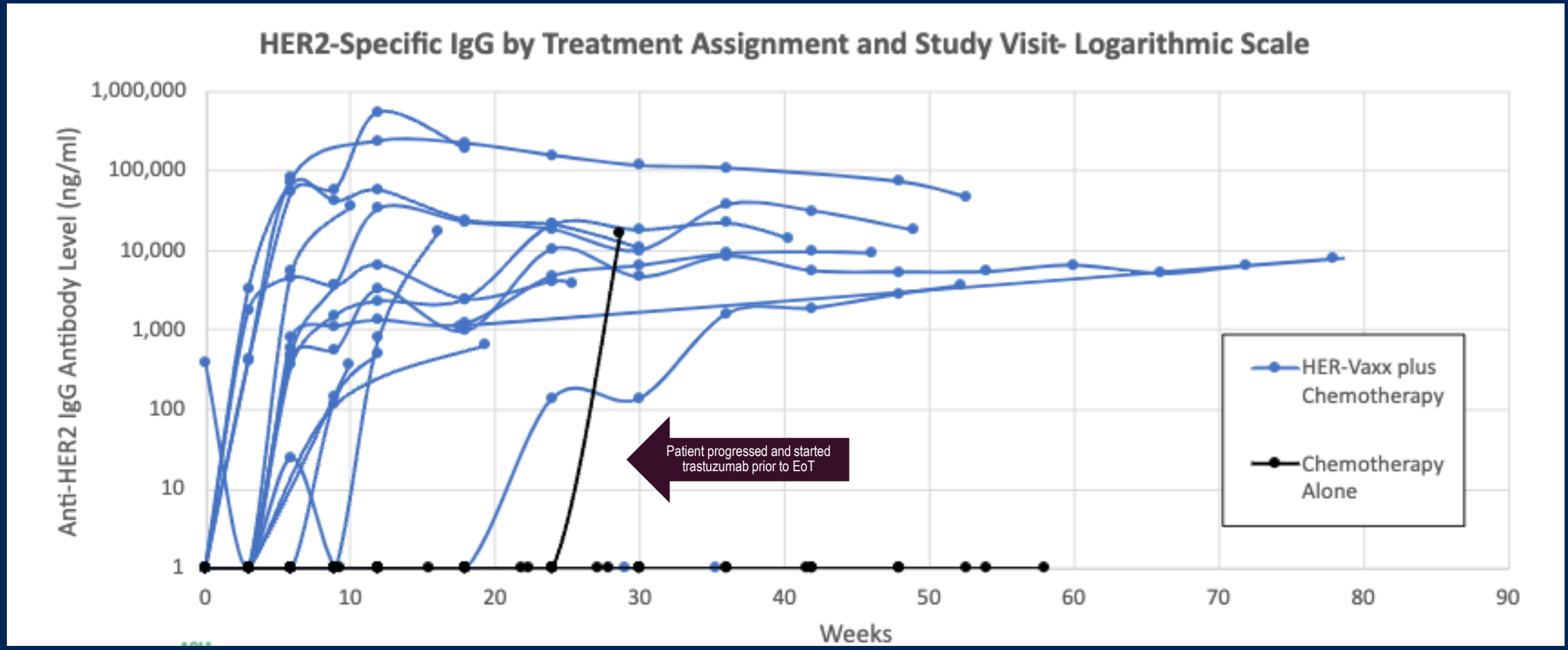




Five patients not included due to: 2 patients with no target lesions; No tumor evaluation by BICR for 1 HER-Vaxx + Chemotherapy (1 PD) and Chemotherapy (1 PR, 2 PD) patients.

Data cut 01Jun22

HER-Vaxx Produced Elevated and Sustained Anti-HER-2 IgG Antibodies



Data cut 01Jun22

Conclusions

- HER-Vaxx (IMU-131) + chemotherapy showed a statistically significant 45% overall survival benefit compared to chemotherapy alone (14.0 vs 8.3 months)
- Duration of response was longer in HER-Vaxx + chemotherapy arm over chemotherapy alone arm (30 vs 19 weeks)
- Vaccination with HER-Vaxx induced persistent HER-2 specific antibodies which correlated with clinical response as proof of concept for a first-in-class B Cell Immunotherapy based on HER-2 peptides
- No additive toxicity was seen when HER-Vaxx was administered in combination with chemotherapy
- Exploring alternative HER-Vaxx doses in single arm phase 2 extension study
- The nextHERIZON study (NCT05311176) is currently enrolling (TIP #16 @ASCO GI): HER-Vaxx plus ramucirumab /paclitaxel OR pembrolizumab following progression with trastuzumab treatment in GC