nextHERIZON: A PHASE 2 STUDY OF HER-VAXX, A HER-2 TARGETING PEPTIDE VACCINE, IN COMBINATION WITH CHEMOTHERAPY OR PEMBROLIZUMAB IN PATIENTS WITH HER-2 METASTATIC OR ADVANCED GASTRIC/GASTROESOPHAGEAL ADENOCARCINOMA WHO PROGRESSED ON OR AFTER TRASTUZUMAB TREATMENT

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IMUGENE
Developing Cancer Immunotherapies

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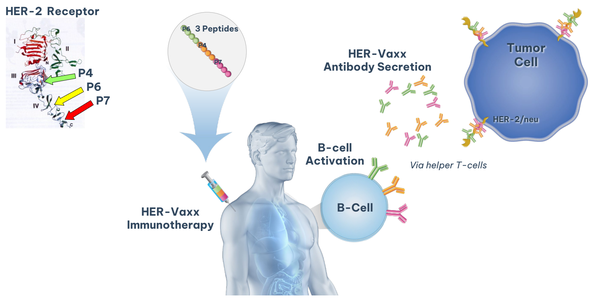
Introduction

- HER-Vaxx is a B Cell Immunotherapy designed to treat tumors that over-express the HER-2/neu receptor, including gastric and breast cancer.
- The immunotherapy is constructed from three B-cell epitopes derived from the extracellular domain of HER-2/neu.
- The Phase 1b study showed that active immunization with HER-Vaxx was well tolerated and induced HER-2-dose dependent immune response corresponding to tumor reduction in advanced gastric cancer (GC) or gastroesophogeal junction (GEJ).
- The Phase 2 HERIZON study revealed a significant survival benefit in patients treated with HER-Vaxx plus chemotherapy compared to chemotherapy alone[2].
- Pre-clinical data demonstrated a synergistic effect with combination of HER-2 and PD-1 vaccines and 90% tumor growth inhibition[3].
- Ramucirumab plus paclitaxel is an approved second-line treatment for patients with GC/GEJ who have failed first-line treatment with chemotherapy or trastuzumab.
- The nextHERIZON study seeks to evaluate the clinical benefit of adding HER-Vaxx to ramucirumab + paclitaxel OR pembrolizumab following progression on or after trastuzumab therapy.

Figure 1

HER-Vaxx Active Immunisation Mechanism of Action



Key Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
✓ Confirmed diagnosis of advanced or metastatic HER-2/neu overexpressing GC or GEJ adenocarcinoma	✗ Systemic chemotherapy or major surgery within 28 days before starting study treatment
✓ Progressed on or after trastuzumab therapy	✗ Arm 2 only: Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent
✓ Measurable disease as per RECIST 1.1 criteria and assessed by the local investigator	✗ Arm 2 only: Has received prior therapy with an ICI or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g., CTLA-4, OX 40, CD137) and was discontinued from treatment due to a grade 3 or higher adverse event
✓ HER-2/neu overexpression (3+ by IHC or if IHC 2+ confirmed by FISH, BDISH, or CISH utilizing post-progression fresh or archival tissue or pathology report)	✗ Prior organ transplantation, including allogenic stem-cell transplantation
✓ Eastern Cooperative Oncology Group (ECOG) performance status 0-1	✗ Chronic immunosuppressive therapy (systemic steroids >10mg or others) within 7 days prior the first dose of study drug
✓ Adequate bone marrow, renal and hepatic function	✗ Active, known, or suspected autoimmune disease

Study Design

TRIAL	PATIENTS	STUDY
• Phase 2 • Open Label • Global • Treat until progression/toxicity	• >1L • Advanced or metatstatic GC/GEJ • HER-2/neu overexpressing • Progressed on or after trastuzumab	• Non-Randomized • HER-Vaxx + ramucirumab + paclitaxel OR • HER-Vaxx + pembrolizumab

mGC/GEJ cancer HER-2/neu overexpressing Progressed on or after trastuzumab & previously received PD-1/ PD-L1 treatment → **Arm 1: HER-Vaxx + ramucirumab + paclitaxel**

mGC/GEJ cancer HER-2/neu overexpressing Progressed on or after trastuzumab → **Arm 2: HER-Vaxx + pembrolizumab**

Figure 2

Treatment Arms

ARM 1: HER-Vaxx + ramucirumab + paclitaxel

28-Day Cycles	Cycle 1				Cycle 2			
Days	1	8	15	22	1	8	15	22
HER-Vaxx administration	💉		💉		💉			
Ramucirumab + paclitaxel		✓	✓	✓		✓	✓	✓

HER-Vaxx administered Day 1 of every 2nd cycle from cycle 3 onwards. Treat to progression. Ramucircumab administered D8, 22 of each cycle. Paclitaxel administered D8, 15, 22 of each cycle. Dose-limiting toxicity is 29 days of treatment. Tumor assessment at Day 43 and every 6 weeks.

ARM 2: HER-Vaxx + Pembrolizumab

21-Day Cycles	Cycle 1				Cycle 2		
Days	1	8	15	22	1	8	15
HER-Vaxx administration	💉		💉		💉		
Pembrolizumab		✓			✓		

HER-Vaxx administered Day 1 of every 3rd cycle from cycle 4 onwards. Treat to progression. Dose-limiting toxicity is 29 days of treatment. Tumor assessment at Day 43 and every 6 weeks.

Study Objectives

Arms Assessed Independently

Primary Safety: Safety and tolerability of HER-Vaxx in combination with chemotherapy (ramucirumab plus paclitaxel) or pembrolizumab

Primary Efficacy: Objective Response Rate of HER-Vaxx in combination with chemotherapy or pembrolizumab

Secondary: Overall Survival, Progression Free Survival, Duration of Response of HER-Vaxx in each Arm

Exploratory:

- Humoral and cellular immunogenicity data of HER-Vaxx plus chemotherapy (ramucirumab plus paclitaxel) or pembrolizumab
- Arm-specific associations of immunogenicity and biochemical markers and efficacy parameters
- Arm-specific associations between clinical outcome and HER-2 expression, PD-L1 expression and tumor mutational burden

Study Information

- Protocol Number: NCT05311176
- Status: Enrolling
- Sites: US, Australia, Taiwan, other countries (TBD)

References

1. Wiedermann, U., et al. Clinical and Immunologic Responses to a B-Cell Epitope Vaccine in Patients with HER2/neu-Overexpressing Advanced Gastric Cancer—Results from Phase Ib Trial IMU.ACS.001. *Clinical Cancer Research* 2021;27(13): 3649-3660.
2. Maglakelidze, M., et al. HERIZON: IMU-131 Peptide Vaccine Plus Standard of Care Chemotherapy in Patients with HER2 Overexpressing Metastatic or Advanced GEJ/GC. European Society of Medical Oncology Asia Congress, December 2-4, 2022; Singapore.
3. Kaumaya PTP, et al. Immunogenicity and antitumor efficacy of a novel human PD-1 B-cell vaccine (PD1-Vaxx) and combination immunotherapy with dual trastuzumab/ pertuzumab-like HER-2 B-cell epitope vaccines (B-Vaxx) in a syngeneic mouse model. *Oncoimmunology*. 2020;9(1):1818437.