



HERIZON: A Phase 2 study of HER-Vaxx (IMU-131), a HER2-targeting peptide vaccine plus standard of care hemotherapy in patients with HER2+ advanced stomach Cancer — dose-dependent anti-cancer antibodies correlating with improved clinical outcome

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Introduction

- HER-2/neu, a member of the epidermal growth factor receptor (EGFR) family, is overexpressed in 6%-30% of gastric cancers.
- HER-Vaxx is a B cell peptide-based anti-HER-2/neu vaccine (IMU-131) comprising trastuzumab's binding site^{1,2}.
- In the phase 1b HERIZON trial (NCT02795988), HER-Vaxx has been shown to be safe and to prolong progression-free survival in patients with HER-2/neu-overexpressing gastric/gastro-esophageal junction cancer (GC)³.
- Results from a phase 2 study showed that treatment with HER-Vaxx lead to a clinical meaningful increase in overall survival when added to standard of care chemotherapy^{4,5}.

Aim

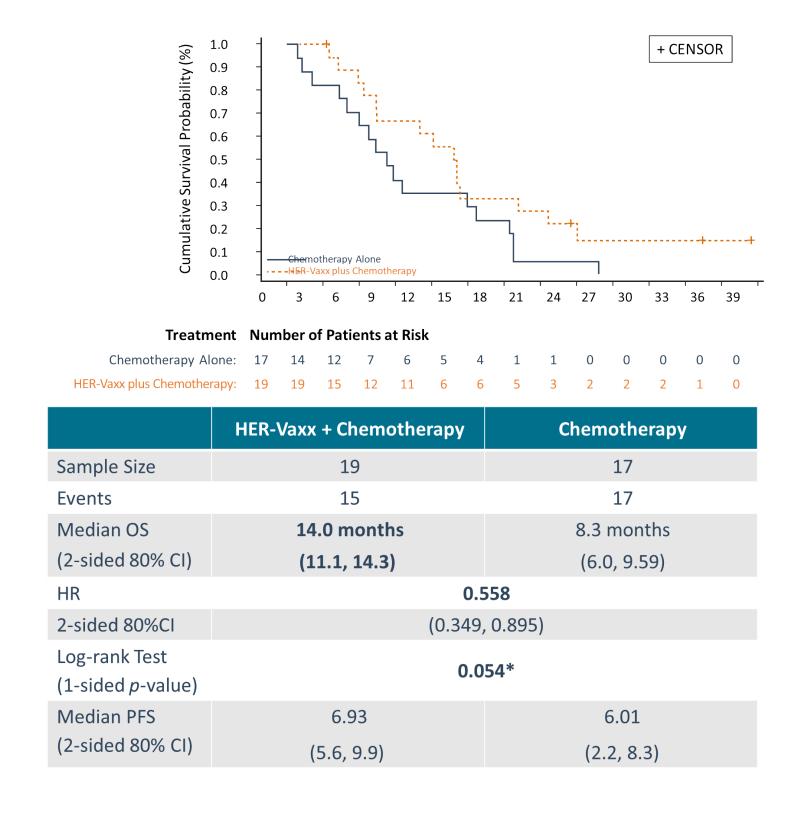
The randomized phase 2 open-label, multi center study included patients with metastatic HER-2 overexpressing GC naïve to HER-2/neu therapy, aimed to evaluate:

- Clinical efficacy of HER-Vaxx plus chemotherapy compared to chemotherapy alone based on overall survival (OS) and progression free survival (PFS)
- Antibody response to HER-Vaxx and their functionality, and the clinical responses

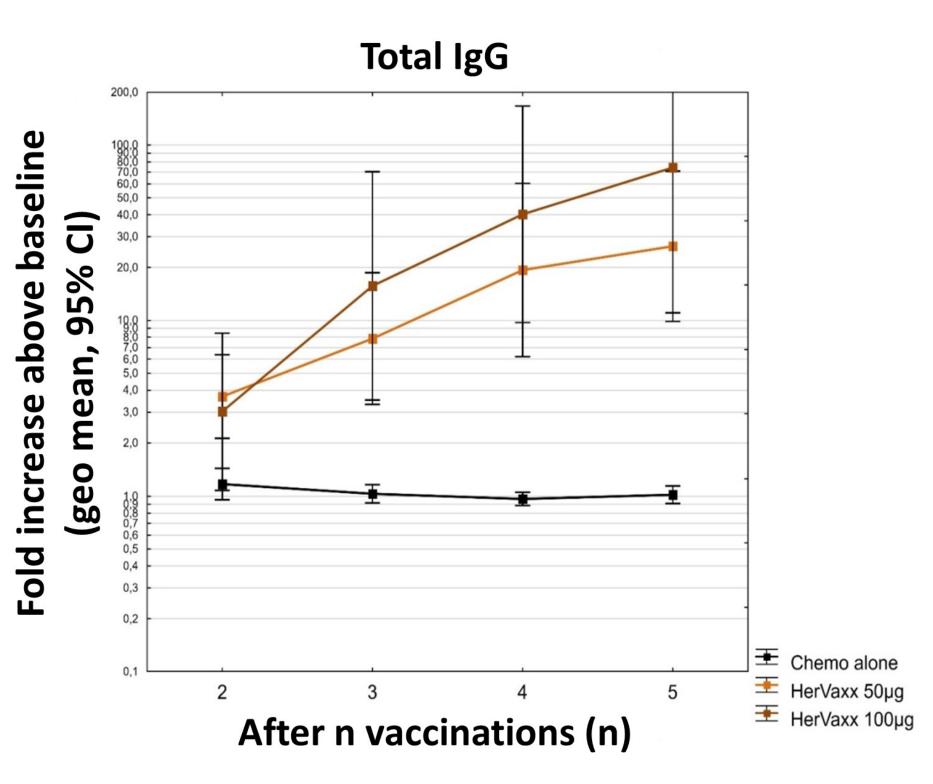
Methods

- Patients were randomized to HER-Vaxx plus chemo (n=19) or chemotherapy alone (n=17), and HER-Vaxx (50μg) was administered on days 0, 14, 35, 77, 140 and q.63 days.
- Clinical response was assessed by RECIST 1.1.
- The levels of serum HER-2/neu-specific IgG and IgG1 and intracellular phosphorylation were assessed by ELISA, and binding levels by FACS

A significant increase in overall survival induced by HER-Vaxx

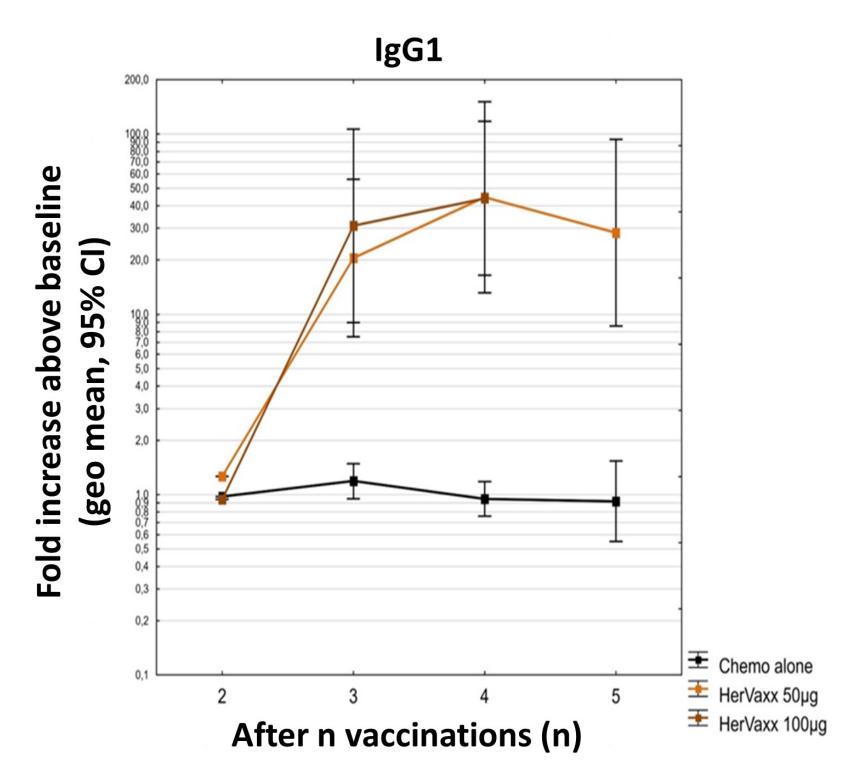


HER-Vaxx induced significant levels of HER-2/neu-specific IgG antibodies

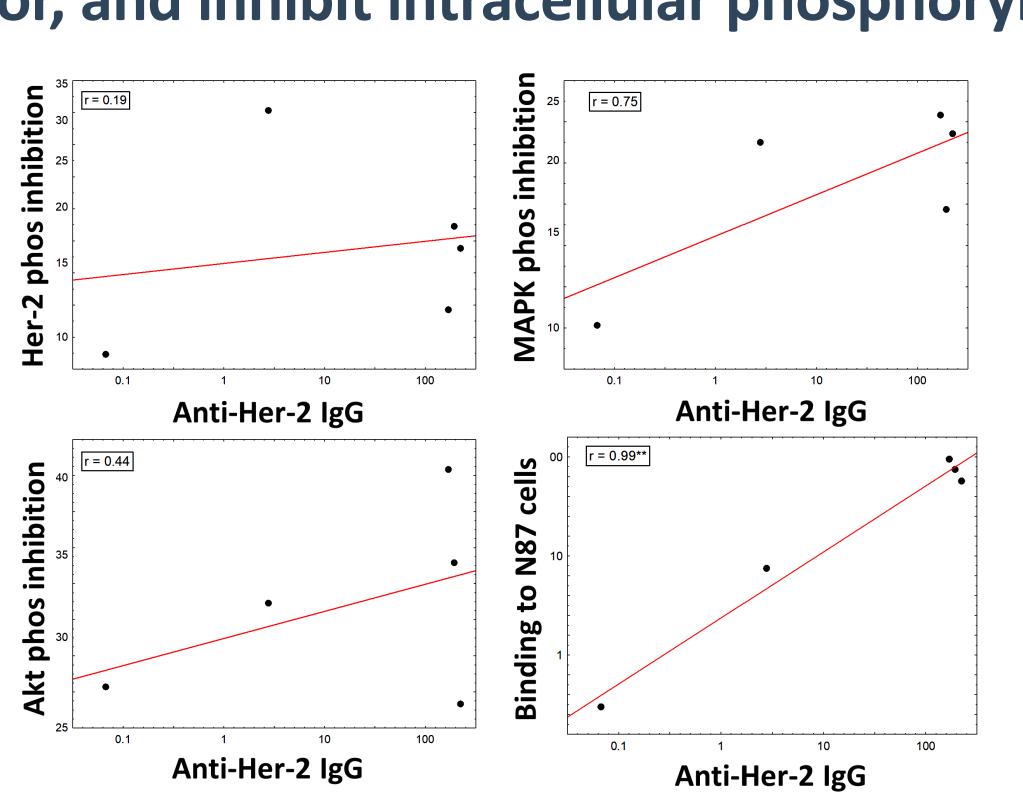


Results

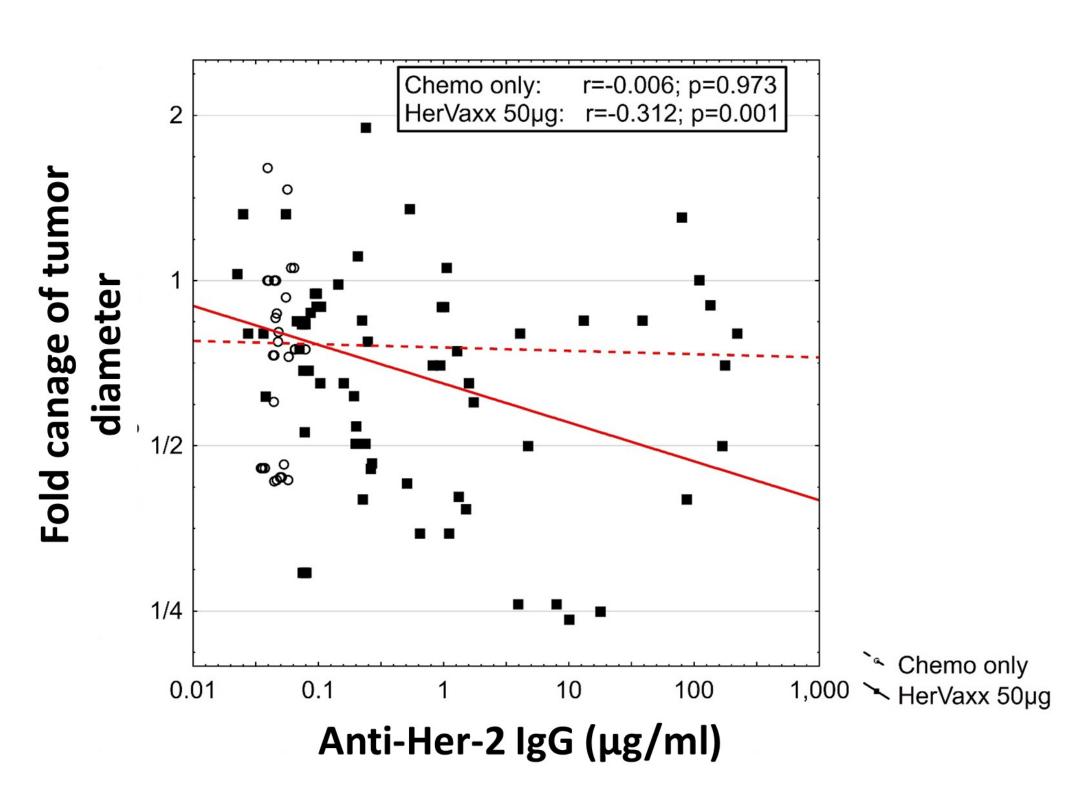
HER-Vaxx induced significant levels of HER-2/neu-specific IgG1 antibodies



The induced Her-2/neu specific IgG antibodies bind to gastric carcinoma cell line expressing the receptor, and inhibit intracellular phosphorylation



HER-Vaxx-induced IgGs correlated with tumor reduction



Conclusions

- Compared to chemotherapy alone, the vaccination resulted in a statistically significant overall survival benefit.
- HER-Vaxx treatment produced robust anti-HER-2-IgG and IgG1 antibody response (p<0.001)
- HER-Vaxx-based vaccination of patients with HER-2-overexpressing GC, induced anti-HER-2-lgG and lgG1 subclass antibody responses (p<0.001) with dose-dependent functionality in binding to Her-2/neu-expressing cells and intracellular phosphorylation of the receptor and the signaling pathway kinases Akt and MAPK.
- The presented data further validate the proof of concept for a first-in-class B-cell immunotherapy based on HER-2/neu peptides.

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. Clin Cancer Res. 2021;27(13), 3649-3660.
- 2. Tobias, J., et al. Enhanced and long-term immunogenicity of a Her-2/neu multi-epitope vaccine conjugated to the carrier CRM197 in conjunction with the adjuvant Montanide. BMC Cancer 2017;17(1), 118.
- 3. Maglakelidze, M., et al. A phase 1b/2 open-label study with randomization in phase 2 of Imu-131 Her2/neu peptide vaccine plus standard of care chemotherapy in patients with Her2/neu overexpressing metastatic or advanced adenocarcinoma of the stomach or gastroesophageal junction. Cancer Research. 2021;81(13_Supplement), CT107-CT107.
- 4. Maglakelidze, M., et.al. HERIZON: A Phase 2 study of IMU-131, a HER2 targeting peptide vaccine, plus standard of care chemotherapy in patients with HER2 overexpressing metastatic or advanced gastric/GEJ adenocarcinoma ESMO Asia Poster. 2022, Singapore.
- 5. Tobias, J., et al. PD-8 HERIZON: A phase 2 study of HER-Vaxx (IMU-131), a HER2-targeting peptide vaccine plus SOC chemotherapy in patients with HER2+ advanced stomach cancer – correlation of the antibody responses and clinical outcome. Annals of Oncology, 2023. 34: p. S4.

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Conflicts of Interest

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