IMUGENE
Developing Cancer Immunotherapies

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Frontline vaccination with the B-cell peptide compound HER-Vaxx (IMU-131), combined with standard-of-care chemotherapy induces high levels of HER2-specific antibodies mediating ADCC and intracellular phosphorylation inhibition resulting in overall survival benefit in patients with HER2+ metastatic or advanced gastric/GEJ adenocarcinoma – Final results from Phase II/HERIZON study

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Introduction

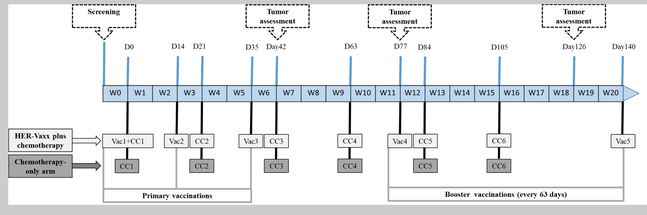
- HER2, a member of the epidermal growth factor receptor (EGFR) family, is overexpressed in 6%-30% of gastric cancers
- HER-Vaxx is a B cell peptide-based anti-HER2 vaccine (IMU-131) comprising binding site of trastuzumab (Herceptin®)[1]
- HER-Vaxx has been shown (Phase Ib, NCT02795988) to be safe and to prolong progression-free survival in patients with HER2-overexpressing gastric/gastro-esophageal junction cancer (GC)[2,3]
- Interim Phase II evaluation of the vaccine has shown a clinically meaningful increase in overall survival when added to standard-of-care chemotherapy[4,5,6]

Aim

This randomized phase II open-label, multi-center study in patients with metastatic/advanced HER2 overexpressing GC aimed to evaluate: * Clinical efficacy (overall survival, progression-free survival) of HER-Vaxx plus chemotherapy compared to chemotherapy alone * Antibody response to HER-Vaxx and their functionality, and correlation with the clinical responses

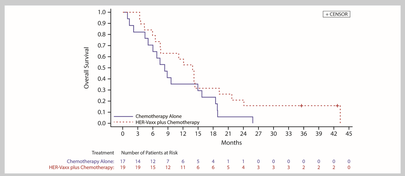
Methods

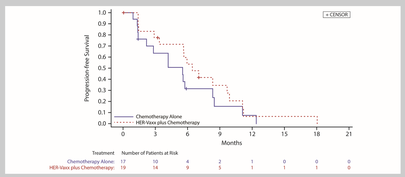
- Patients were randomized to chemotherapy alone (n=17) or HER-Vaxx together with chemotherapy (n=19).
- Clinical response was assessed by RECIST 1.1.
- ELISA, ADCC and flow cytometry assays were applied for the assessment and characterization of the HER-Vaxx-induced antibodies



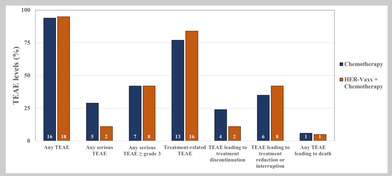
Results

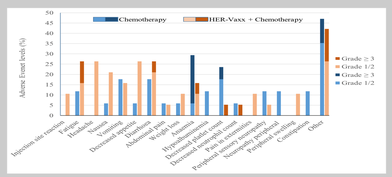
HER-Vaxx increased OS and PFS



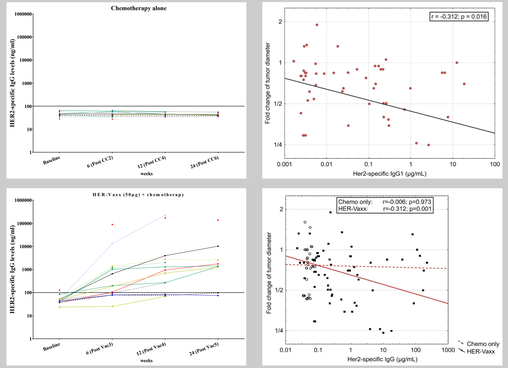


HER-Vaxx was not associated with safety concerns

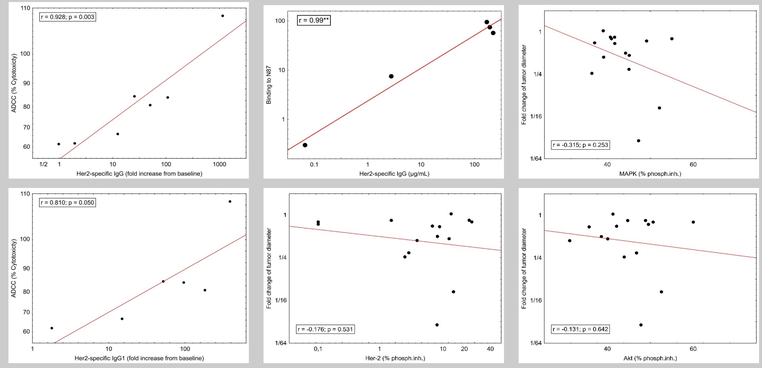




HER-Vaxx induced significant levels of HER2-specific IgG and IgG1 antibodies correlating with tumor size reduction



HER-Vaxx induced antibodies mediating ADCC, binding to HER2-expressing gastric carcinoma cells, and inhibiting intracellular phosphorylation



Conclusions

- **Compared to chemotherapy alone, vaccination with HER-Vaxx was associated with a 40% overall survival benefit**
- **No additive vaccine-associated toxicity was observed**
- **HER-Vaxx treatment produced robust anti-HER2-IgG and IgG1 antibody response ($p<0.001$)**
- **HER-Vaxx induced HER2-specific antibodies able to mediate antibody-dependent cell cytotoxicity (ADCC) and inhibit intracellular HER2 phosphorylation, and correlated with tumor reduction**
- **Our reults further validate the proof of concept for a first-in-class B-cell immunotherapy based on HER2 peptides.**

References

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