

Outcome prediction of Her-2/neu targeting therapies in humans by pre-clinical evaluation in mice? Vaccination with a multi-peptide B cell vaccine targeting Trastuzumab and Pertuzumab binding sites, suggests a combination with PD-L1-targeting therapy

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Introduction

We have developed a B cell-based hybrid peptide Her-2/neu vaccine (HerVaxx) comprising Trastuzumab's binding site. In clinical evaluations HerVaxx has shown to reduce primary tumor growth by inducing polyclonal anti-tumor immune responses and immunological memory.

Aim

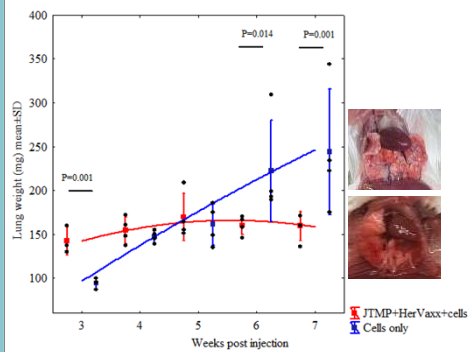
Trastuzumab and Pertuzumab improve the clinical outcome of patients with Her-2/neu positive metastatic breast cancer. Thus, we aimed to evaluate prevention of metastasis formation in vivo by a multi-peptide B cell vaccine containing HerVaxx and pertuzumab's mimotope/B cell epitope (JTMP).

Methods

Mice were vaccinated with the multi-peptide vaccine and tail-vein injected with mammary carcinoma cells expressing human Her-2/neu.

Preclinical setting

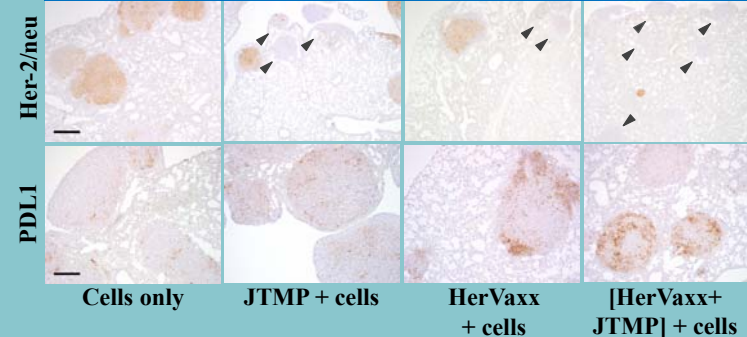
Significant reduction of lungs metastasis



Vaccination of tumor cells-injected mice with the multi-peptide vaccine comprising HerVaxx and pertuzumab's mimotope (JTMP) significantly reduces lungs weight and metastasis.

Tobias et al, 2022, Transl. Oncol.

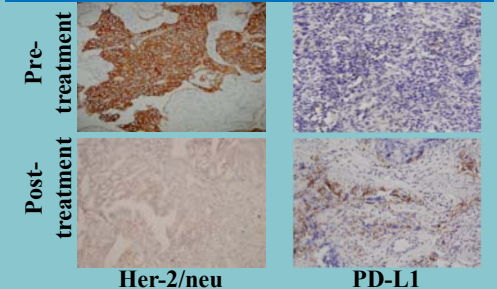
Loss of Her-2/neu and upregulation of PD-L1 expression



Vaccination of tumor cells-injected mice with HerVaxx, the mimotope (JTMP) of pertuzumab or in particular the combination of both vaccines induce loss of Her-2/neu and upregulation of PD-L1 expression

Clinical setting

HerVaxx induces loss of Her-2/neu and upregulation of PD-L1 expression



In one patient enrolled in the highest dose cohort of our Phase 1b trial (50 µg; Wiedermann et al, 2021, Clin. Cancer Res), treatment with our vaccine HerVaxx induces loss of Her-2/neu and upregulation of PD-L1 expression in the patient's primary tumor (Submitted).

Conclusions

- Our multi-peptide B cell Her-2/neu vaccine may serve as a secondary intervention in adjuvant settings to prevent metastasis and tumor spread
- Targeting Her-2/neu results in upregulation of PD-L1 expression, as also observed in clinical setting with HerVaxx, implying a combination therapy targeting PD-L1
- A combination therapy targeting both Her-2/neu and PD-L1 could be adapted to the stage and progression phase of the disease to potentially result in the remission of the metastases.

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* Conflicts of interest: The presenter, Tobias J., declares no potential conflicts of interest.

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** The study was supported by a research grant from Imugene (Australia) to the Medical University of Vienna.