Phase II trial of HER2-PET/CT using ^{68}Ga-anti-HER2 VHH1 for characterization of HER2 presence in brain metastases of breast cancer patients

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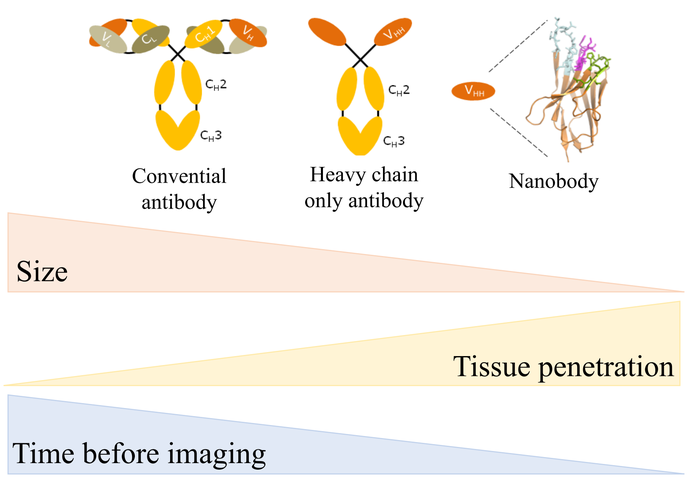
Background

Brain metastases are challenging in breast cancer patients, especially in HER2+ patients whose peripheral metastases can often be controlled using standard-of-care HER2 regimens. Relapse or progression in the brain can determine survival for such patients. **Tumour microenvironment** is an important factor with respect to drug penetration and might influence the therapeutic effect.

The anti-HER2 agent is a single-domain antibody or nanobody that targets HER2 with nanomolar affinity but with **a size that is ten-fold smaller** than conventional antibodies. This could be an important factor in **diagnostic and even therapeutic efficacy for nanobody radiopharmaceuticals.**

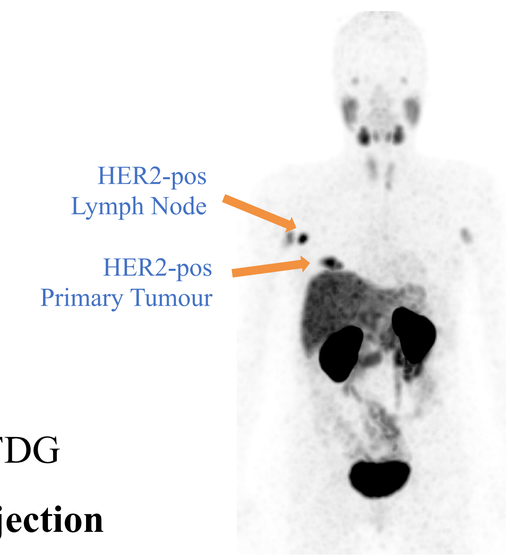


Trial design

- Open label non-randomized monocenter phase II trial
- Breast cancer patients with **brain metastasis of min. 8mm**
- Injection of 37-185 MBq ^{68}Ga-anti-HER2 VHH1
- Full body PET/CT scan at **90 min post injection**
- Evaluation of tumour targeting potential in brain metastases
- HER2 amplification reassessed on blood-derived cell-free DNA.
- A total of 30 patients (10 HER2-NEG, 20 HER2-POS)

Prior Phase I trial results

- Safe and well tolerated
- **Good visualisation of LN and M+**
- Variable visualisation of primary T
- Liver uptake decreases up to 90 min
- Kidney uptake and clearance via urine
- **Low irradiation burden**, comparable to FDG
- Imaging best performed at **90 min post injection**



Preliminary results

HER2-positive disease

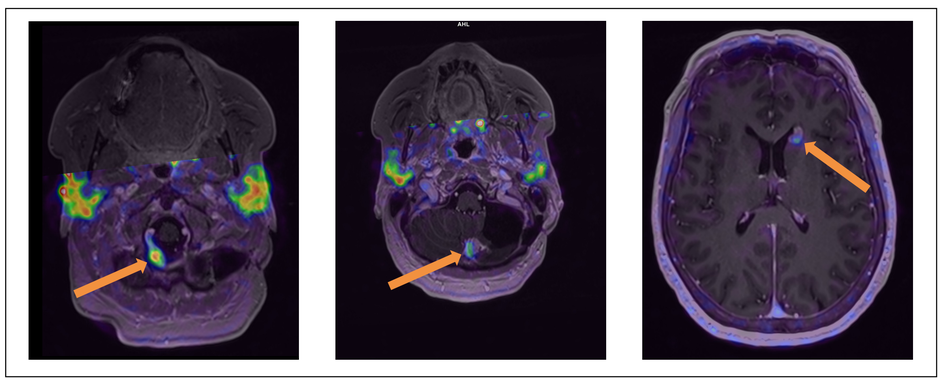


Figure 1: Leptomeningeal disease in a patient with HER2-positive breast cancer accumulation of the HER2-tracer in multiple locations of disease.

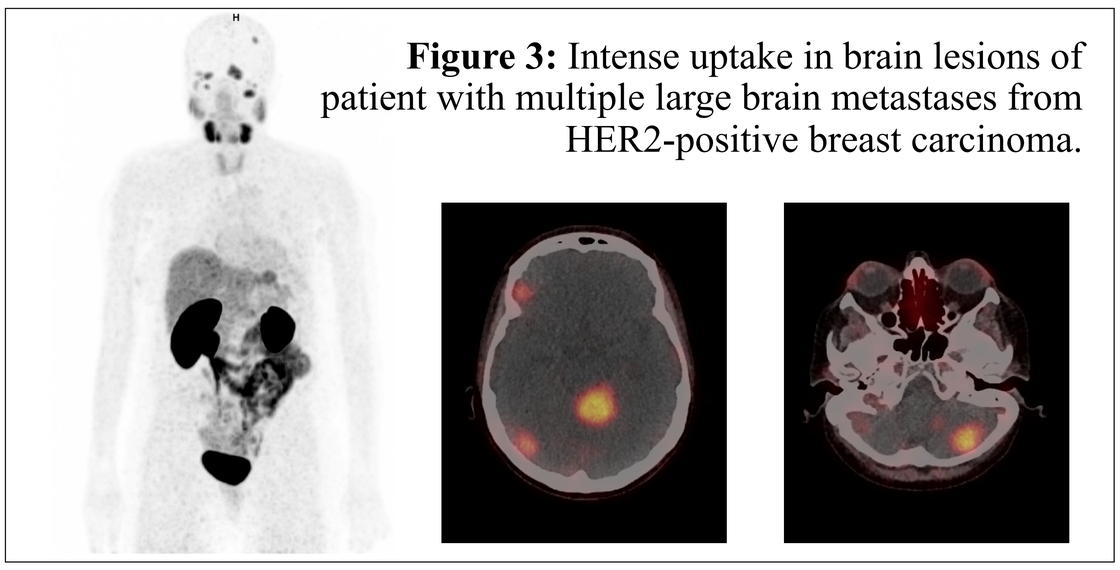


Figure 3: Intense uptake in brain lesions of patient with multiple large brain metastases from HER2-positive breast carcinoma.

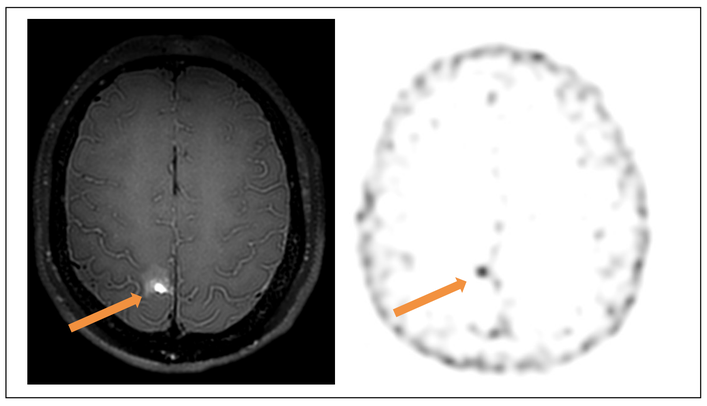


Figure 2: brain lesion of 8 mm after external beam radiation poses a differential diagnosis between radionecrosis and disease recurrence. The HER2-tracer shows accumulation in the lesion, and MRI after 3 months confirmed disease progression.

HER2-negative disease

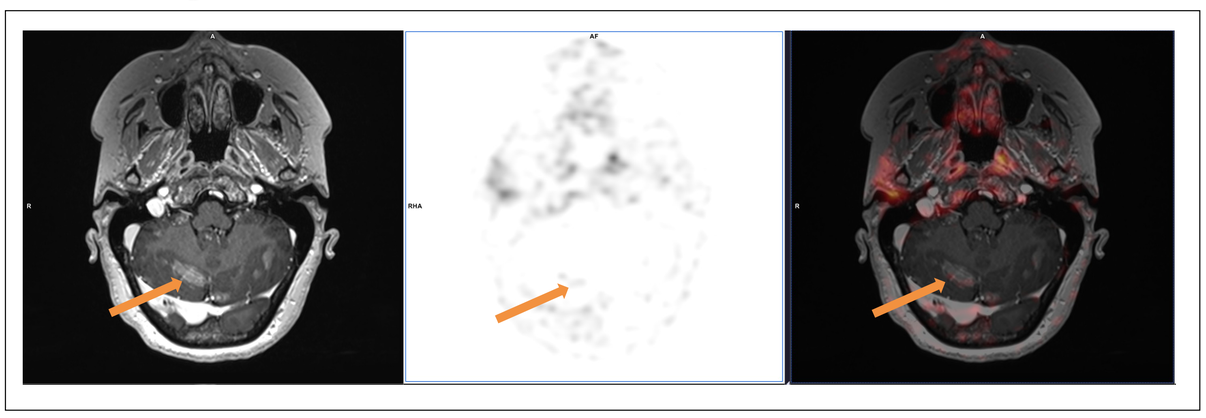


Figure 4: Leptomeningeal disease in a patient with HER2-negative breast cancer confirms very low tracer accumulation in known lesion. MRI, PET and PET/MRI fusion from left to right.

Clinical trial identification

EudraCT 2015-002328-24, NCT03331601

Conflict of Interest

MK, TL, CX have patents on Nanobody imaging and Therapy. MK received travel and accommodation expenses from Bayer. TL is co-founder of and employed by of Camel-IDS, received honoraria from IBA and Institut des Radioéléments (IRE). MK and VC received research funding from Camel-IDS.

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