Imaging of CD8+ cytotoxic T-cells by \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) PET/MRI: First clinical experience in patients with metastatic cancer

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INTRODUCTION

CD8+ cytotoxic T cells are key players in anti-cancer immune responses as they destroy MHC class I-dependent tumor cells. Therefore, the spatial distribution of CD8+ cytotoxic T cells might represent an important surrogate for the response to cancer immunotherapy including immune checkpoint inhibitor therapy ICT. The radiolabeled minibody \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) is characterized by a high affinity to human CD8 and was already investigated in a phase I study. Here, we present our first experience with the non invasive in vivo assessment of the whole body CD8 T cell distribution in cancer patients using clinical \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) PET/MRI.

METHODS

In total 8 patients with metastasized cancers (5 x malignant melanoma; 1 x choroidal melanoma, 1 x NSCLC and 1 x sarcoma) were studied before (n = 3) or during (n = 5) ICT. Multiparametric PET/MRI was performed 24 h after injection of 74.2 ± 19.7 MBq \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) on a Siemens Biograph mMR System (Siemens Healthineers, Erlangen, Germany). The whole body distribution of the \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) tracer was analyzed with a special focus on tumors/metastases as well as primary and secondary lymphatic organs.

RESULTS

The PET tracer \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) was well tolerated without any reported side effects. The PET/MRI acquisitions 24 h.p.i. of \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) revealed a comparably low background signal with only a minor contribution of unspecific tissue retention. Regarding the primary and secondary lymphoid organs we observed a high interpatient variability of the tracer uptake. Four out of five patients with previous ICT exhibited a relatively high \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) uptake in the bone marrow. Also a large number of non metastatic lymph nodes yielded a pronounced \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) uptake in four patients. Strikingly, a low \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) uptake in the spleen compared to the liver was observed in 4 out of the 5 patients with cancer progression during ICT. Interestingly, only one metastasis with an intense tracer was detected in this patient cohort.

CONCLUSION & OUTLOOK

These first clinical experiences revealed the feasibility to assess potential immune-related changes by \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) PET/MRI. Considering these results we hypothesize that the whole body distribution of CD8+ cytotoxic T-cells assessed by non-invasive in vivo \([^{89}\text{Zr}]\text{Zr-Df-IAB22M2C}\) PET/MRI might be associated with the response to cancer immunotherapy which needs to be investigated in subsequent prospective trials.

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