A novel theranostic concept for Adrenocortical Neoplasia targeting the chemokine receptor CXCR4

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Background: The chemokine receptor CXCR4 is a key factor for tumour growth and metastasis in several human cancers. Recently, [^{68}Ga]Pentixafor has been developed as a tracer for positron emission tomography specifically targeting CXCR4.

Methods: Chemokine receptor expression was evaluated by quantitative PCR and immunohistochemistry in normal adrenals and in adrenocortical carcinoma tissue (115 primary tumours, 19 local recurrences and 16 metastases) and correlated with clinical data. The diagnostic value of the newly established PET tracer [^{68}Ga]Pentixafor, a specific CXCR4 ligand, was assessed in 21 patients with advanced adrenocortical carcinoma (ACC). The precursor (Pentixafor) was kindly provided by Scintomics (Fürstenfeldbruck, Germany); radiolabelling with ^{68}Ga and subsequent PET/CT imaging was performed on a compassionate use base at the Dept. of Nuclear Medicine, University Hospital Würzburg. Imaging results were compared to [^{18}F]FDG PET/CT.

Results: We observed significant CXCR4 membrane staining in 83% of investigated tumour tissue sections of primary tumours and metastases of ACC with a trend towards a shorter disease free survival in tumours with high CXCR4 expression. [^{68}Ga]Pentixafor-PET imaging detected tumour lesions in ACC patients with high sensitivity. Visual comparison with [^{18}F]FDG-PET resulted in comparable findings in 7 (32%) patients. In one patient (5%) [^{68}Ga]Pentixafor identified more metastatic lesions, and in 4 patients (19%) complementary information was obtained by [^{68}Ga]Pentixafor and [^{18}F]FDG-PET regarding the number and uptake of lesions. CXCR4 expression as detected by [^{68}Ga]Pentixafor-PET-CT was rated sufficiently high to consider CXCR4-directed therapy in 67% of the included patients.

Conclusion: CXCR4 is highly expressed in most ACCs, potentially contributing to the malignant behaviour of this neoplasia. neoplasia. [^{68}Ga]Pentixafor-PET provides excellent imaging sensitivity based on high and specific tracer accumulation in ACC lesions, paving the way for pentixafor-based CXCR4-targeted radiotherapy in this malignancy.