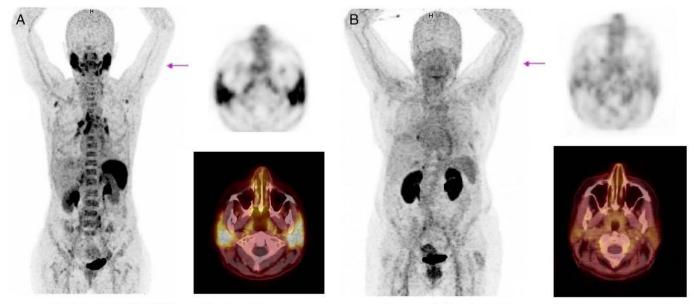
Chemokine Receptor 4 Expression in Primary Sjögren's Syndrome

Wojciech Cytawa, MD, PhD,*† Stefan Kircher, MD, PhD,‡ Andreas Schirbel, Dr Rer. Nat. PhD,* Takahiro Shirai,§ Kazuhito Fukushima, MD, PhD,* Andreas K. Buck, MD, PhD,* Hans-Jürgen Wester, MD, PhD,// and Constantin Lapa, MD, PhD*

Abstract: ⁶⁸Ga-pentixafor is a novel radioligand of C-X-C motif chemokine receptor 4. A 55-year-old woman with a history of primary Sjögren's syndrome underwent ⁶⁸Ga-pentixafor PET/CT for staging of lymphoma originating from mucosa-associated lymphoid tissue. Whereas no lymphoma manifestation could be detected, imaging revealed bilateral intense radiotracer uptake in both parotid and submandibular salivary glands, consistent with inflammatory cell infiltration.

REFERENCES

- Domanska UM, Kruizinga RC, Nagengast WB, et al. A review on CXCR4/ CXCL12 axis in oncology: no place to hide. *Eur J Cancer*. 2013;49:219–230.
- Herhaus P, Habringer S, Vag T, et al. Response assessment with the CXCR4directed positron emission tomography tracer [⁶⁸Ga]pentixafor in a patient with extranodal marginal zone lymphoma of the orbital cavities. *EJNMMI Res.* 2017;7:51.
- Demmer O, Gourni E, Schumacher U, et al. PET imaging of CXCR4 receptors in cancer by a new optimized ligand. *ChemMedChem*. 2011;6:1789–1791.
- Herrmann K, Schottelius M, Lapa C, et al. First-in-human experience of CXCR4-directed endoradiotherapy with ¹⁷⁷Lu- and ⁹⁰Y-labeled pentixather in advanced-stage multiple myeloma with extensive intra- and extramedullary disease. J Nucl Med. 2016;57:248–251.
- Lapa C, Herrmann K, Schirbel A, et al. CXCR4-directed endoradiotherapy induces high response rates in extramedullary relapsed multiple myeloma. *Theranostics*. 2017;7:1589–1597.
- Bluemel C, Hahner S, Heinze B, et al. Investigating the chemokine receptor 4 as potential theranostic target in adrenocortical cancer patients. *Clin Nucl Med.* 2017;42:e29–e34.
- 7. Werner RA, Weich A, Higuchi T, et al. Imaging of chemokine receptor 4 expression in neuroendocrine tumors—a triple tracer comparative approach. *Theranostics*. 2017;7:1489–1498.
- Lapa C, Reiter T, Werner RA, et al. [⁶⁸Ga]Pentixafor-PET/CT for imaging of chemokine receptor 4 expression after myocardial infarction. *JACC Cardiovasc Imaging*. 2015;8:1466–1468.



Patient with Sjögren's syndrome

Patient with physiologic CXCR4 expression

FIGURE 1. C-X-C motif chemokine receptor 4 (CXCR4) plays an important role in the process of tumor growth and formation of metastasis but also coordinates trafficking and homing of leukocytes toward sites of inflammation.^{1,2} ⁶⁸Ga-pentixafor is a novel radioligand of CXCR4, ^{3,4} which has been used for noninvasive in vivo receptor visualization in both oncologic^{5–7} and inflammatory conditions.⁸ A 55-year-old woman with a history of primary Sjögren's syndrome underwent ⁶⁸Ga-pentixafor (SCINTOMICS GmbH, Fürstenfeldbruck, Germany) PET/CT for staging of extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue, primarily diagnosed in minor salivary glands of the lower lip. Whereas no further mucosa-associated lymphoid tissue manifestation could be detected, imaging revealed bilateral intense radiotracer uptake (SUVmax 10.9) in both parotid and submandibular salivary glands (A), consistent with inflammatory cell infiltration (for comparison, average SUVmax of parotid glands in 15 other asymptomatic patients was 1.8 ± 0.4, an example in B). Noteworthy, increased CXCR4 expression in the spleen (A; SUVmax 9.7) was noticed, most likely to chronic B-cell stimulation. Bilaterally increased ⁶⁸Ga-pentixafor accumulation (A; SUVmax 8.0) in mediastinal, hilar, and axillary lymph nodes was histologically proven as due to benign infiltration of polyclonal leukocytes. This report further supports the feasibility of CXCR4-directed imaging for the detection of inflammatory activity. ⁶⁸Ga-pentixafor PET/CT might prove a useful tool for the noninvasive evaluation, as well as therapy monitoring of autoimmune diseases and other inflammatory/infectious conditions.