A 64-year-old female with primarily diagnosed small cell lung cancer was referred to our department for positron emission tomography (PET)/computed tomography work-up with [18F]FDG and [68Ga]Pentixafor, a radiotracer for CXC-motif chemokine receptor 4, with the latter being performed on a compassionate use basis in compliance with Section 37 of the Declaration of Helsinki, the German Medicinal Products Act, AMG Section 13 2b, and in accordance with the responsible regulatory body (Regierung von Oberfranken) to check for a potential therapeutic option in this patient. Diagnosis had been established 4 weeks earlier when the patient presented to the emergency room with new-onset aphasia (word retrieval). Cerebral magnetic resonance imaging revealed a contrast-enhancing mass in the left temporal region, which was histopathologically confirmed as small cell lung cancer metastasis.

The day after brain surgery, the patient experienced acute ischemic stroke in the right posterior cerebral artery territory. At the day of presentation to our nuclear medicine department, she reported on recovering hemianopia, and no other neurological symptoms could be recorded.

Concerning the suspected lung carcinoma, both PET modalities visualized a solitary lesion in the upper lobe of the right lung, highly consistent with the suspected primary (Figure 1). In the central nervous system, however, imaging with [18F]FDG-PET demonstrated markedly reduced glucose metabolism in the infarction area, whereas CXC-motif chemokine receptor 4–directed PET visualized concordantly increased receptor expression (Figure 2).

Recently, proof-of-concept for visualization of CXC-motif chemokine receptor 4 expression by [68Ga]Pentixafor, a radiolabeled, highly human-specific receptor ligand for PET imaging, has been demonstrated in patients with small cell lung cancer and other (hematologic) diseases. Although the feasibility of [68Ga]Pentixafor PET imaging has not been studied in experimental models of ischemic stroke yet, the stromal cell–derived factor 1α/CXC-motif chemokine receptor 4 axis has been shown to play an important role in the recruitment of inflammatory and stem and progenitor cells to the areas of ischemic injury after both myocardial infarction and ischemic stroke. Its noninvasive, in vivo visualization might lead to novel insights into the course and prognostic implications of posts ischemic inflammatory response.

Disclosures
Dr Wester is the founder and shareholder of Scintomics. S. Kropf is CEO of Scintomics. The other authors report no conflicts.

References

Keywords: aphasia ◼ CXCR4 ◼ positron emission tomography ◼ small cell lung carcinoma ◼ stroke
Figure 1. Display of representative axial slices of computed tomography (CT, A) and [18F]FDG- (B) and CXCR4 (C)-directed positron emission tomography (PET). All modalities present a pulmonary lesion in the right upper lobe, highly consistent with lung cancer. CXCR indicates CXC-motif chemokine receptor.

Figure 2. Cerebral magnetic resonance imaging (cMRI) at day 2 after brain surgery shows demarcation of right posterior ischemia with corresponding changes in diffusion-weighted images (A, b value = 1000 s/mm²) and apparent diffusion coefficient values (B). [18F]FDG-PET demonstrates significantly reduced tracer uptake in the infarction area (C). In contrast, [68Ga]Pentixafor-PET (one day later) visualizes upregulation of CXCR4 (D, Inset; maximum intensity projection; standardized uptake value max = 4.08 versus standardized uptake value mediatinal bloodpool = 1.62), which correlates with cMRI changes (E, DWI/PET fusion). CXCR indicates CXC-motif chemokine receptor; DWI, diffusion-weighted image; and PET, positron emission tomography.
[\textsuperscript{68}Ga]Pentixafor–Positron Emission Tomography/Computed Tomography Detects Chemokine Receptor CXCR4 Expression After Ischemic Stroke
Jan Stefan Schmid, Andreas Schirbel, Andreas K. Buck, Saskia Kropf, Hans-Jürgen Wester and Constantin Lapa

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