

Twins in spirit: DOTATATE and high-affinity DOTATATE

Claudia Brogsitter · Margret Schottelius · Klaus Zöphel ·
Jörg Kotzerke · Hans-Jürgen Wester

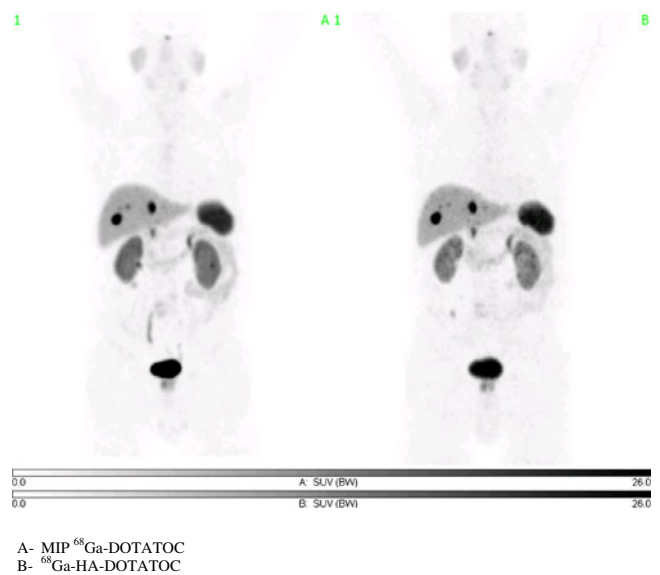
Received: 26 April 2013 / Accepted: 18 June 2013 / Published online: 21 August 2013
© Springer-Verlag Berlin Heidelberg 2013

Since the introduction of somatostatin receptor (sst) imaging using ^{123}I -Tyr³-octreotide [1], peptide receptor imaging and radiotherapy (PRRT) has become an established modality in the management of neuroendocrine tumours (NET) [2].

Based on the findings of a previous study [3] investigating metal-labelled DOTA-octreotides substituted at Tyr³, we hypothesized that derivatives of DOTA-iodo-Tyr³-octreotide might be excellent candidates for sstr imaging and therapy. Consequently, we evaluated ^{68}Ga -DOTA-iodoTyr³-octreotide (^{68}Ga -HA-DOTATATE; HA, high affinity) in vitro and in a preliminary PET study. As hypothesized, ^{68}Ga -HA-DOTATATE showed high affinity for human sst_{2,5} as well as diagnostic and logistical advantages, i.e. unlimited precursor availability. The (Leu⁸,D-Trp²², [^{125}I]Tyr²⁵)-SST28 IC₅₀ values (in nanomoles) for Ga-HA-DOTATATE were >10,000 (sst1), 0.64 ± 0.23 (sst2), >1,000 (sst3 and sst4) and 59.7 ± 15.1 (sst5), and for Ga-DOTATATE were >10,000 (sst1), 0.67 ± 0.25 (sst2), >1,000 (sst3), 822 ± 327 (sst4) and >1,000 (sst5).

In a first PET study a 73-year-old patient suffering from a NET with unknown primary and liver metastases was investigated with ^{68}Ga -HA-DOTATATE and ^{68}Ga -DOTATATE. Both agents showed a possible small primary tumour in the midgut and five liver metastases that showed somewhat higher ^{68}Ga -HA-DOTATATE uptake (mean SUV_{max} 23.8 vs. 21.6). The visual detectability of three small liver metastases with low uptake was superior with ^{68}Ga -HA-DOTATATE.

In summary, ^{68}Ga -HA-DOTATATE provides high-quality images comparable to or better than those with ^{68}Ga -DOTATATE. Further clinical studies are needed to confirm these first results and explore the use of HA-DOTATATE agents for PRRT.



References

1. Krenning EP, Bakker WH, Breeman WA, Koper JW, Kooij PP, Ausema L, et al. Localisation of endocrine-related tumours with radioiodinated analogue of somatostatin. *Lancet*. 1989;1:242–4.
2. Zaknun JJ, Bodei L, Mueller-Brand J, Pavel ME, Baum RP, Horsch D, et al. The joint IAEA, EANM, and SNMMI practical guidance on peptide receptor radionuclide therapy (PRRT) in neuroendocrine tumours. *Eur J Nucl Med Mol Imaging*. 2013;40:800–16.
3. Ginj M, Schmitt JS, Chen J, Waser B, Reubi JC, de Jong M, et al. Design, synthesis, and biological evaluation of somatostatin-based radioligands. *Chem Biol*. 2006;13:1081–90.

C. Brogsitter · K. Zöphel · J. Kotzerke (✉)
Klinik und Poliklinik für Nuklearmedizin, Universitätsklinikum
Carl Gustav Carus, Technische Universität Dresden, Dresden,
Germany
e-mail: joerg.kotzerke@mailbox.tu-dresden.de

M. Schottelius · H.-J. Wester
Pharmaceutical Radiochemistry and Department of Nuclear
Medicine, Technische Universität München, Munich, Germany