Journal of Nuclear Medicine, published on December 20, 2018 as doi:10.2967/jnumed.118.223453

Dear Editor and readers,

We would like to thank Dr. Kotzerke and his colleagues for the important insights into the uptake of DOTA-EB-TATE, an albumin-binding octreotate developed by us (1-4). The results presented Dr. Kotzerke are of high importance, suggesting that the radiometal chelated into the DOTA moiety affects the uptake and perhaps binding of both DOTA-TATE and EB-DOTA-TATE. The authors concluded that "As a consequence of the different uptakes, only different isotopes of the same element (like $^{86}Y/^{90}Y$ or $^{64}Cu/^{67}Cu$) can be used for the assessment of biokinetic data".

Although the data presented by the authors are intriguing, we would like to argue that: (1) These results are not specific to EB-DOTA-TATE but are seen with DOTA-TATE as well. It is common practice to use ^{68}Ga-DOTA-TATE to detect tumor SSTR2 expression before radionuclide therapy with ^{177}Lu-DOTA-TATE and so far, this practice seems to prove itself. Moreover, ^{68}Ga-DOTA-TATE scan has significantly lower radiation exposure to the patient than other longer-lived isotopes labeled same ligand. It would be unreasonable in our opinion to use ^{86}Y for imaging when a much safer option is available. (2) The authors derive their conclusion from *in vitro* cell uptake and extrapolated the result to predict the *in vivo* pharmacokinetics. It would be more appropriate to draw a more conclusion from actual *in vivo* studies.

We look forward to seeing data from a more in-depth *in vivo* studies done, perhaps, by Dr. Kotzerke and colleagues.

References:

1. Tian R, Jacobson O, Niu G, et al. Evans Blue Attachment Enhances Somatostatin Receptor Subtype-2 Imaging and Radiotherapy. Theranostics. 2018;8(3):735-745.
2. Bandara N, Jacobson O, Mpoy C, Chen X, Rogers BE. Novel Structural Modification Based on Evans Blue Dye to Improve Pharmacokinetics of a Somastostatin-Receptor-Based Theranostic Agent. Bioconjug Chem. 2018;29:2448-2454.
3. Zhang J, Wang H, Jacobson O, et al. Safety, Pharmacokinetics, and Dosimetry of a Long-Acting Radiolabeled Somatostatin Analog 177Lu-DOTA-EB-TATE in Patients with Advanced Metastatic Neuroendocrine Tumors. J Nucl Med. 2018;59:1699-1705.
4. Wang H, Cheng Y, Zhang J, et al. Response to Single Low-dose 177Lu-DOTA-EB-TATE Treatment in Patients with Advanced Neuroendocrine Neoplasm: A Prospective Pilot Study. Theranostics. 2018;8:3308-3316.

Orit Jacobson, Xiaoyuan Chen*
Laboratory of Molecular Imaging and Nanomedicine (LOMIN)
National Institute of Biomedical Imaging and Bioengineering (NIBIB)
National Institutes of Health (NIH)
*Shawn.Chen@nih.gov