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LETTER TO THE EDITOR

Additional information on "Direct comparison of the in vitro and in vivo stability of DFO, DFO* and DFOcyclo* for ^{89}Zr-immunoPET"

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Dear Sir,

Following the publication of our article entitled "Direct comparison of the in vitro and in vivo stability of DFO, DFO* and DFOcyclo* for ^{89}Zr-immunoPET" in EJNMMI [1], readers sent us some remarks and questions. In this letter, we would like to address these questions by providing additional information about our study.

- DFOcyclo* is derived from DFO and not from DFO*. In DFO*, the trihydroxamate DFO is elongated with an extra hydroxamate group, exactly the same as present in DFO. In DFOcyclo*, the DFO is elongated with a cyclic hydroxamate group having a different linker length.
- During the manuscript review process, DFO*-NCS was made commercially available at ABX (catalogue number 7272). Therefore, the following statement in the introduction "However, in the absence of an improved, clinically applicable chelator, there is room for more efficient [^{89}Zr]Zr^{4+} chelators" is no more correct.
- The stability assays were performed in PBS at pH 7.4.
- The amounts of DFO and EDTA used for the challenge experiments were calculated based on the amount of chelators.
- DFOcyclo* was used as a racemate in the experiments reported in the article.
- The results depicted in Figs. 4c and 5a are based on two different sets of experiments. Initially the in vivo stability of [^{89}Zr]Zr-DFOcyclo*-trastuzumab was compared with [^{89}Zr]Zr-DFO-trastuzumab, of which the results are depicted in Fig. 4c. Once we observed an improved in vivo stability of [^{89}Zr]Zr-DFOcyclo*-trastuzumab, a subsequent in vivo study was performed to investigate its stability compared with [^{89}Zr]Zr-DFO*-trastuzumab as well (Fig. 5). Although aimed at similar experimental conditions, the use of a freshly thawed cell line and new mice could have caused heterogeneity between the two experiments (e.g., increased tumor growth rates which result in different interstitial pressures that could affect the %ID/g), which could explain the slight differences in tumor uptake, blood kinetics, and uptake in other organs.

This article is part of the Topical Collection on Radiopharmacy

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Compliance with ethical standards The authors declare that they have no conflict of interest. This article does not contain any studies with human participants.

Reference

1. Raavé R, Sandker G, Adumeau P, Jacobsen CB, Mangin F, Meyer M, et al. Direct comparison of the in vitro and in vivo stability of DFO, DFO* and DFOcyclo* for 89Zr-immunoPET. Eur J Nucl Med Mol Imaging. 2019;46(9):1966–77. https://doi.org/10.1007/s00259-019-04343-2.