

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tau-23-674>

Comment 1: Reviewer A

A well written and timely piece highlighting the emergence of radiohybrid ligands. This should be of great interest to the journals readers and hopefully ignite further studies in this area to optimise the use and availability of this technology.

Reply 1: Thank you for your encouraging feedback.

Changes in the text: None required.

Comment 1: Reviewer B

The correct terminology is [18F]rhPSMA-17.3, [18F]DCFPyL, [68Ga]Ga-PSMA-11. Google EANM nomenclature.

Reply 1: Dear Reviewer Thank you for your comments, we have updated the draft accordingly.

Changes in the text: Entire text updated to the standard nomenclature mentioned above.

Comment 2: Reviewer B

The author should note that transport of radiotracer is not required for centres with an existing gallium generator.

Reply 2: Thank you, we have added this to the text.

Changes in the text: Mentioned Paragraph 2 “easier transportation from production site to the clinic when applicable”

Comment 3: Reviewer B

The author could consider to discuss studies that directly compare [18F]rhPSMA-17.3 and [18F]DCFPyL or [68Ga]Ga-PSMA-11 as the latter two are more established tracers for PSMA PET,

Reply 3: Thank you for your valuable comments, the original publication from LIGHTHOUSE that we commenting upon specifically mentions that not to compared it directly with the other agents, however, we have used few references other studies with the established agents and discussed them indirectly.

Changes in the text: None

Comment 1: Reviewer C

Describe the molecules used in the clinical study in more detail, including molecular structures and describing the molecular mechanism of action, as well as the advantage that might result by employing these molecules for both diagnostic and therapeutic use.

Reply 1: Dear reviewer - thank you very much for providing these comments. We have added some additional detail regarding the molecular structure and mechanism of action (e.g., the Glu-Urea-Lys/Glu binding motif with similar action to other clinical radiopharmaceuticals). We have also added a brief line to indicate rhPSMA can be labeled with an 18F imaging agent or chelated to a metal (imaging or therapeutic image). Due to limitations in word count, we did not include more detail, but we would be happy to do so if you think anything else is missing.

Changes in the text: Complete paragraph no 2 has been significantly updated to reflect these changes.

Comment 2: Reviewer C

Clinical data resulting from the study are commented on and evaluated but no PET images are shown about what is described.

Reply 2: Thank you for your comments, we have added few images for reference.

Changes in the text: Images added to the text.

Comment 3: Reviewer C

It is not clear what the end point of the clinical study is.

Reply 3: Thank you, we have elaborated on the primary endpoints

Changes in the text: First paragraph updated and the primary co endpoints are elaborated further

Comment 4: Reviewer C

Explain the clinical-therapeutic-drug framework in which the use of this molecule is embedded.

Reply 4: Thank you for your comments, we have revised test and added a refence with potential clinical benefit to high radiation delivery to tumors for treatment with less radiation to the urinary tract.

Changes in the text: Paragraph 4 last 5 lines revised

Comment 5: Reviewer C

Compared to the title of the article, I expected a more articulate and detailed description of this type of molecule Radiohybrid PSMA ligand.

Reply 5: Thank you again for these comments regarding rhPSMA. We have added some more discussion regarding rhPSMA. If there is more you think we should add, we would be happy to. Thank you again.

Changes in the text: Updated paragraph 2.

Comment 6: Reviewer C

Increase the number of literature references (at least 25-30).

Reply 6: Thank you for your valuable comments, we would have wanted to add more however, in order to adhere with the word limits we are only able to add essential citations.

Changes in the text: Added one more reference.
