



## 2021: the year [<sup>177</sup>Lu]Lu-PSMA-617 RLT PSMA is ready for incorporation into clinical guidelines?

Reply to “A perspective on the EANM procedure guidelines for radionuclide therapy with <sup>177</sup>Lu-labelled PSMA-ligands” by Dr. Geromo Gericke

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Dear Sir,

Thank you very much for giving us the opportunity to comment on the important aspects raised by Dr. Gericke.

The intention of the “EANM procedure guidelines for radionuclide therapy with <sup>177</sup>Lu-labelled PSMA-ligands (<sup>177</sup>Lu-PSMA RLT)” is to give guidance to centers intending to implement PSMA-targeted radioligand therapy prior to availability of an approved compound [1]. While not clearly defined the labelling as “procedure guideline” aims to describe the process of patient selection, application and follow-up. It is not intended to discuss or to draw definitive conclusions on efficacy comparing different therapies, which is in the scope of randomized clinical trials. The preamble of procedure guidelines clearly defines a flexible framework and significant impact of advances in knowledge or technology subsequent to publication of the guidelines on clinical practice. The recently published TheraP data as well as the press release by Novartis raise the expectations that soon prospective phase 3 data will be available justifying the inclusion of [<sup>177</sup>Lu]Lu-PSMA-617 RLT into clinical (as compared to procedure) guidelines [2, 3].

The mentioned statement “exchangeable application of PSMA-617 and PSMA-I&T” clearly relates to the mode of application, the expected toxicity profile and the known dosimetry data. We fully agree with Dr. Gericke that there is no comparative data available, nor does the limited body of available data allow for a reliable clinical comparison of biodistribution.

Dr. Gericke also questions whether the statement “data indicate a favourable safety profile for <sup>177</sup>Lu-PSMA RLT” can be generalized across various ligand molecules. Despite the tremendously higher number of patients historically treated with [<sup>177</sup>Lu]Lu-PSMA-617, there are nevertheless more than 100 patients treated with [<sup>177</sup>Lu]Lu-PSMA-I&T reported in the literature [4].

Regarding the comment of Dr. Gericke on the “efficacy” part, we concur that with the recently published data by Hofman et al. as well as the soon expected VISION trial data, [<sup>177</sup>Lu]Lu-PSMA-617 is the only compound that has, for now, clinical supportive evidence for efficacy [2, 3]. Accordingly, the integration of [<sup>177</sup>Lu]Lu-PSMA-617 into clinical guidelines can be expected.

The authors want to reemphasize that a procedural guideline is intended to assist Nuclear Medicine practitioners in performing, interpreting and reporting procedures which are either not yet or — from a procedural standpoint — not adequately represented in clinical guidelines. Procedural guidelines do not intend to give recommendations regarding clinical efficacy or clinical superiority. To adequately clarify this, an EANM wide definition and standardization of the various types of guidelines are under its way.

Moreover, the authors fully support and welcome the activity of AAA/Novartis in the field of radioligand therapy and fully echo the commitment to adhere to scientific standards, precise interpretation of available information, or lack thereof, and timely updates as new information becomes available. The unique space of radioligand therapy strongly benefits

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from strong academia efforts in developing novel concepts potentially accelerating the access of cancer patients to new effective therapies. However, this space also needs the expertise, credibility and track record of newly and well-established pharmaceutical companies to allow for worldwide approval and access to radioligand therapy. The current growth of radioligand therapy will only be sustainable if the investments made will be economically rewarded — for Nuclear Medicine, this means if an approved drug is available, it has to be used clinically.

In summary, we hope we have successfully clarified the intent and scope of the  $^{177}\text{Lu}$ -PSMA RLT procedure guideline [1]. In anticipation of the presentation of the VISION results, the authors sincerely are convinced that the use of [ $^{177}\text{Lu}$ ]Lu-PSMA-617 RLT will soon find its way into clinical guidelines.

**Code availability (software application or custom code)** Not applicable.

**Author contribution** Not applicable.

**Data availability** Not applicable.

## Declarations

**Ethics approval** Institutional Review Board approval was not required for this Letter to the Editor.

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**Consent for publication** Not applicable.

**Conflict of interest** The authors are active Nuclear Medicine practitioners and true believers in theranostics. Ken Herrmann reports personal fees from Bayer, personal fees and other from Sofie Biosciences, personal fees from SIRTEX, non-financial support from ABX, personal fees from Adacap, personal fees from Curium, personal fees from Endocyte, grants and personal fees from BTG, personal fees from IPSEN, personal fees from Siemens Healthineers, personal fees from GE Healthcare, personal fees from Amgen, personal fees from Novartis, personal fees from ymabs, personal fees from Aktis Oncology, personal fees from Theragnostics and personal fees from Pharma15, outside the submitted work. Clemens Kratochwil is a co-inventor of the PSMA-617 patent.

Wolfgang P. Fendler was a consultant for BTG, and he received fees from RadioMedix, Bayer and Parexel outside of the submitted work. Matthias Eiber reports prior consulting activities for Blue Earth Diagnostics, Progenics Pharmaceuticals and Point Biopharma and a patent application for rhPSMA outside of the submitted work. No further conflicts of interest in regard to this letter to the editor.

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