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Tumor Sink effect: Myth or Reality?

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TO THE EDITOR: We thank Prive et al. for their correspondence (*1*). As acknowledged in our publication (*2*), the main limitation of the study is the use of a single time-point SUV measurement as a surrogate for radiation dose. Differential PSMA uptake patterns and tumor to background ratios are observed when PSMA PET image acquisition is performed at late timepoints in comparison to images acquired at 1-hour post-injection (*3-6*). Thus it is clear that images acquired 1-hour post-injection cannot reflect the biological effects of ^{177}Lu-PSMA that occur over more than 3 weeks (biological half-life). However, even if not perfectly accurate, PSMA PET imaging performed at 1 hour still provides a fair estimate of the patient target expression and of the biodistribution of a PSMA-targeted radiopharmaceutical and prior studies have reported that pre-therapeutic PSMA PET measurements may be correlated with radiation dose to tumor and normal organs from Lu177-PSMA therapy (*7-9*).

Regarding the definition of low- and high-volume disease, it is important to note that CHAARTED and LATTITUDE criteria were defined based on conventional imaging (*10*). Applying these criteria for an analysis of PSMA PET can lead to major discordance in patient stratification, as described previously (*11*). Therefore we recommend to explicit use the term “PSMA-VOL” in reference to the whole-body PSMA PET volumetric assessment and not just “low-volume” or “high-volume” metastatic, as follows: PSMA-VOL very-low (<25 ml), PSMA-VOL low (25-189 ml), PSMA-VOL very-low (<25 ml), PSMA-VOL moderate (189-532 ml), PSMA-VOL high (532-1355 ml) and PSMA-VOL very high (≥ 1355 ml).

As the authors mention, we agree that patients with low-volume metastatic disease or oligometastases can safely benefit from PSMA-based radionuclide therapy without decreasing the commonly used dose-activity level of 7.4 GBq per cycle currently in-use in the ongoing trial NCT04443062 and as supported by preliminary data (*12*). On the other hand our results suggest that the dose-activity level of ^{177}Lu-PSMA could be increased safely in patients with very high PSMA-VOL (≥1355 ml). Nevertheless, these findings warrant further validation by dosimetry studies and safety assessments in prospective clinical trials.

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