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¹⁷⁷Lu-rhPSMA-10.1 Induces Tumor Response in a Patient With mCRPC After PSMA-Directed Radioligand Therapy With ¹⁷⁷Lu-PSMA-I&T

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Abstract: ¹⁷⁷Lu-rhPSMA-10.1 is a novel PSMA-targeting radiopharmaceutical that has been optimized in terms of pharmacological and pharmacokinetic properties and may be therefore advantageous in treatment of metastatic castrate-resistant prostate cancer. In this image, we present the case of an 86-year-old man with metastatic castrate-resistant prostate cancer undergoing ¹⁷⁷Lu-PSMA-I&T treatment. After initial partial response to radioligand therapy, another 2 treatment cycles resulted in a rising serum PSA level that could be correlated with increasingly PSMA-positive as well as a new bone lesion. Consequently, the patient was changed to ¹⁷⁷Lu-rhPSMA-10.1 treatment on a compassionate use basis achieving a renewed tumor response.

Key Words: theranostics, ¹⁷⁷Lu-rhPSMA-10.1, prostate cancer, radioligand therapy

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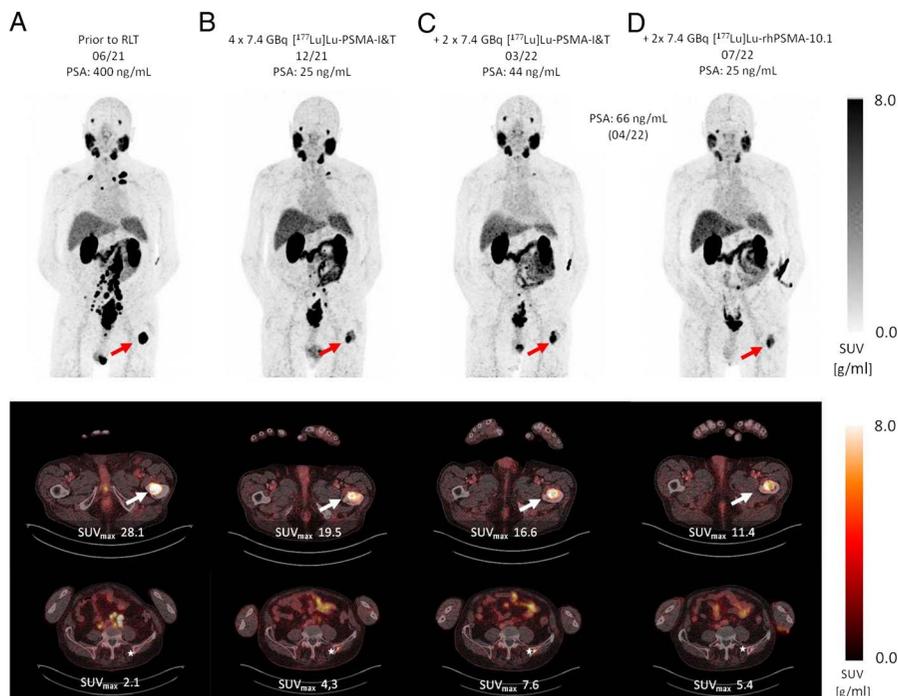


FIGURE 1. An 86-year-old man with metastatic castrate-resistant prostate cancer (mCRPC) and biochemical progression was referred for further theranostic workup. Previously, he had undergone androgen deprivation therapy including LHRH agonists (buserelin) and novel androgen axis drugs (enzalutamide) as well as taxane-based chemotherapy (docetaxel and cabazitaxel). PET/CT using ^{68}Ga -PSMA-I&T^{1,2} revealed local recurrence as well as multiple (pelvic, retroperitoneal, supraclavicular) lymph node and bone (eg, left femur, arrows) metastases (A). Subsequently, PSMA-directed radioligand therapy was recommended according to recent practice^{3,4} and the decision of the institutional interdisciplinary tumor conference. After 4 cycles with ^{177}Lu -PSMA-I&T (B), a biochemical as well as radiologic partial response was noted. Treatment was continued for another 2 cycles. At restaging, in contrast to the continued response in the local as well as the lymphonodal tumor manifestations, increasing PSMA expression of metastases in the left femur (arrows) and left iliac wing (stars) as well as a new lesion in lumbar vertebra 5 was recorded, consistent with rising PSA serum values (C). Given the lack of further therapeutic options, 2 additional cycles of radioligand therapy with ^{177}Lu -rhPSMA-10.1 were offered on a compassionate use basis resulting in a renewed tumor response (D). Radiohybrid prostate-specific membrane antigen (rhPSMA) ligands are a new class of radiopharmaceuticals in prostate cancer theranostics.^{5–7} Pretherapeutic dosimetry with one agent from this class (^{177}Lu -rhPSMA-7.3C) has recently shown (on an inpatient basis) tumor uptake to be approximately 2.5 times higher than with ^{177}Lu -PSMA-I&T.⁸ Building on this observation, ^{177}Lu -rhPSMA-7.3C has been optimized in terms of pharmacological and pharmacokinetic properties yielding ^{177}Lu -rhPSMA-10.1 that is now being investigated in clinical trials (NCT05413850).

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