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### Safety and Efficacy of [177Lu]Lu-rhPSMA-10.1 Re-Challenge Therapy in Progressive mCRPC after [177Lu]Lu-PSMA I&T Therapy: Preliminary Results

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***Aim/Introduction:*** [$^{177}$Lu]Lu-rhPSMA-10.1 is a new PSMA derivative that has shown promising results in dosimetric studies for the treatment of metastatic castration-resistant prostate cancer (mCRPC) with a higher therapeutic index as compared to [$^{177}$Lu]Lu-PSMA I&T. Therefore therapy re-challenge with [$^{177}$Lu]Lu-rhPSMA-10.1 is a viable therapeutic option after initial disease progression under treatment with [$^{177}$Lu]Lu-PSMA I&T. This study aims to determine the feasibility, efficacy, and safety of [$^{177}$Lu]Lu-rhPSMA-10.1 re-challenge therapy. ***Materials and Methods:*** Eight patients (age, 73±7 years) with progressive mCRPC after previous 2-6 cycles of standard [$^{177}$Lu]Lu-PSMA I&T were subsequently treated with up to two cycles of [$^{177}$Lu]Lu-rhPSMA-10.1 every 6 weeks. Response assessment with

[$^{68}$Ga]Ga-PSMA-I&T-PET/CT using RECIP 1.0 criteria was done after 2 cycles or if disease progression was clinically suspected. PSA response was assessed according to the PCWG3 criteria 8-12 weeks after the first [$^{177}$Lu]Lu-rhPSMA-10.1 cycle. Safety was evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0 criteria. ***Results:*** Mean per cycle and cumulative administered activities were 7.4 ± 0.04 GBq and 13.9 ± 2.3 GBq, respectively. Generally, therapy was well tolerated with no acute adverse events. According to CTCAE v5, grade 4 thrombocytopenia and grade 3 anemia occurred in one patient, in the remaining subjects, no relevant toxicity (> grade 2) was observed. Regarding serum PSA values, biochemical partial response, stable disease, and progressive disease were seen in 1/8 (12.5%), 4/8 (50%), 3/8 (37.5%) patients. RECIP 1.0 criteria revealed disease stabilization in 4/8 (50 %) subjects with partial remission in one individual (12.5 %) and stable disease in 3/8 (37.5%) cases. Outcome data in terms of PFS and OS are still pending at the time present. ***Conclusion:*** Despite very limited numbers, the results of this study suggest that [$^{177}$Lu]Lu-rhPSMA-10.1 may induce therapeutic effects in mCRPC patients who have experienced progressive disease under [$^{177}$Lu]Lu-PSMA I&T. Further studies to corroborate these preliminary findings are highly warranted.