Final results of a prospective phase 2 pilot trial of 177Lu-PSMA 617 (LuPSMA) in men with castrate resistant metastatic prostate cancer (mCRPC), with correlations to baseline PET results.

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Background: ^{177}LuPSMA 617 (LuPSMA) is an emerging therapy in men with metastatic castrate resistant prostate cancer (mCRPC). Paired theranostic agents have the potential to visually identify phenotypes that will respond to targeted therapy. This study examined the value of ^{68}Ga(PSMA-11)(PSMA) PET in predicting treatment response and disease progression in Lu-PSMA therapy within the context of a phase 2 prospective pilot trial.

Methods: Men with mCRPC, who had failed androgen blockade, failed/ ineligible/refused chemotherapy, with GaPSMA positive disease were enrolled in a prospective phase 2 trial. All men underwent LuPSMA therapy 6-8Gbq, 4 doses at 6 weekly intervals. Imaging with FDG, GaPSMA, bone scan and CT scans was at screening, at subsequent PSA rise, or 3 months post completion of 4 cycles of therapy. All men underwent screening imaging with F18Fluorinedeoxuglucose (FDG) and Ga68 PSMA-11 (PSMA) PET CT scans, in addition to staging bone scan and CT chest, abdomen and pelvis.

Results: 14/18 men screened underwent Lu-PSMA therapy. All men completed a minimum 2 cycles of 177Lu PSMA treatment; 3/14 completed 2 cycles, 8/14 completed 3 cycles and 3/14 completed all 4 cycles. One of the 3 patients who completed only 2 cycles discontinued treatment following an exceptional response. Otherwise, treatment was ceased for disease progression in 8/14 men, an unrelated post-operative complication in 1/14 and significant bone pain at the time of therapy in 1/14. 71% (10/14) had a PSA response (mean reduction 59%). A ≥ 50% reduction in PSA occurred in 5/14 (36%), and ≥ 30% in 9/14 (64%). PSMA PET standardised uptake value (SUV) at screening was predictive of ≥ 30% PSA reduction: SUV max 17 ± 9 vs. 44 ± 15 ($p < 0.007$), and PSMA SUV mean 6 ± 4 vs. 10 ± 4 ($p < 0.04$). FDG parameters alone, volume or site of disease did not predict PSA response. No imaging parameters predicted ≥ 50% PSA reduction. Soft tissue response to treatment with RECIST criteria on CT was measurable in 7/14 men, and using bone scan and CT in 10/14 men. Partial response was observed in 4/10, stable disease in 2/10 and progressive disease in 4/10. Mean OS was 50 weeks ± 33 (56 ± 38 responders vs. 36 ± 8 non responders).

Conclusions: PSMA PET has an important role in predicting treatment response to Lu PSMA and in identifying subsequent patterns of failure, which may aid in determining next best treatment options.

Conflicts of Interest: No authors report any relevant conflicts of interest

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