

Patterns of failure on Ga PSMA (GaPSMA) and F18 FDG (FDG) PET CT in a prospective phase 2 trial of 177Lu DKFZ PSMA 617 (LuPSMA) in men with castrate resistant metastatic prostate cancer (mCRPC).

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Background: LuPSMA is emerging as an effective therapy in mCRPC, with retrospective series reporting high PSA response rates in men undergoing treatment (tx). However, not all men have prolonged tx responses. We report the prospective imaging (GaPSMA/FDG) and PSA response of men who progress biochemically during LuPSMA tx to gain information on characteristics of failure patterns, to determine optimal future tx strategies.

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 6-8Gbpq, 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.

Results: 14 men met eligibility criteria and enrolled. 4/14 (28%) men had progressive disease (no PSA response). 10/14 (72%) PSA reduced by a mean 56%. Overall 9/14 (64%) men had >30% decline in PSA, and 5/15(36%) >50% reduction in PSA. 7/15 men were reimaged with GaPSMA, FDG at biochemical failure or 3/12 post tx completion. Imaging revealed 4 distinct patterns (P) of progression.

Conclusions: PSMA acts as both target for radionuclide therapy and biomarker for effective tx response. PSMA and FDG imaging at PSA failure following or during LU PSMA therapy identifies phenotypic patterns of failure that have implications for determining next best tx options in men with mCRPC.

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