TPS5110 Poster Session

Study protocol: Phase 2 trial of re-treatment with 177Lu-PSMA-617 molecular radiotherapy for metastatic castration resistant prostate cancer (RE-LuPSMA trial).

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Background: The phase III VISION trial demonstrated that ^{177}Lu-PSMA-617 radioligand therapy (RLT) improved overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC) who previously received taxane-based chemotherapy and at least one androgen receptor pathway inhibitor (ARPI). As a result, ^{177}Lu-PSMA-617 therapy has been approved in this patient population by the U.S. Food and Drug Administration for up to six cycles (7.4 GBq per cycle) every 6 weeks. Unfortunately, this treatment is not curative and patients relapse even after initially favorable responses. When this occurs, patients have limited treatment options given they have had prior chemotherapy and ARPI regimens. Re-administration of ^{177}Lu-PSMA-617 in patients who previously benefited from therapy and had limited toxicity seems to be a promising option. Small retrospective studies have reported favorable outcomes. Further prospective data with larger sample sizes are needed to confirm these findings. **Methods:** RE-LuPSMA is an investigator-initiated, single-arm, single-center, open-label, phase 2 clinical trial (NCT06288113). This study plans to enroll 40 patients with progressive mCRPC who previously completed 4-6 cycles of ^{177}Lu-PSMA-617 therapy with a favorable response. Favorable response is defined as a prostate-specific antigen (PSA) decline ≥50% during the first regimen. Progression following the first regimen is defined using imaging or PSA (two consecutive PSA increases ≥3 weeks apart). Patients who received another line of prostate cancer therapy within two months of completing the first regimen of ^{177}Lu-PSMA-617 are excluded. Patients must meet PSMA PET/CT VISION criteria. PSMA PET/CT must have been completed within 8 weeks of the planned first cycle of re-challenge therapy. Upon enrollment, participants will receive up to 6 additional cycles of ^{177}Lu-PSMA-617 (7.4GBq every 6 weeks). Patients will follow-up every 6 months until 2 years from the end of re-challenge therapy. The primary endpoint is 12-month OS measured from the start of re-challenge therapy. The study will have 80% power to detect a difference between the null hypothesis of 50% and the study hypothesis of 71%. Secondary endpoints include adverse event rates, PSA response rates (proportion of patients with a PSA decrease of ≥50%), biochemical progression-free survival (time until PSA level increases 25% and 2 ng/mL above the nadir), radiographic progression-free survival, and health-related quality of life changes (measured using Functional Assessment of Cancer Therapy - Radionuclide Therapy [FACT-RNT] and Brief Pain Inventory [Short Form]). Enrollment has started with a planned study duration of 4 years of which subject accrual occurs in the first 12 months. Clinical trial information: NCT06288113. Research Sponsor: UCLA Ahmanson Translational Theranostics Division; Novartis.