TPS5127 Poster Session

PSMA-delay castration (DC): An open-label, multicenter, randomized phase 3 study of [^{177}Lu]Lu-PSMA-617 versus observation in patients with metachronous PSMA-positive oligometastatic prostate cancer (OMPC).

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Background: Androgen deprivation therapy (ADT) ± androgen receptor pathway inhibitor therapy is a primary treatment for metastatic hormone-sensitive prostate cancer, but is noncurative and has significant toxicities when used long-term. In patients with OMPC for whom delaying ADT is appropriate, metastasis-directed therapy such as stereotactic body radiation therapy (SBRT) has been shown to provide local disease control. However, many patients do not experience a complete prostate-specific antigen (PSA) response and develop poly-metastatic disease. [^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA-617) is a prostate-specific membrane antigen (PSMA)-targeted radioligand therapy with demonstrated efficacy and a manageable safety profile in patients with PSMA-positive metastatic castration-resistant prostate cancer in the VISION and PSMAfore trials. PSMA-DC (NCT05939414) is an ongoing, international, randomized phase 3 trial to evaluate the efficacy of ^{177}Lu-PSMA-617 versus observation after SBRT in delaying castration and disease progression in patients with PSMA-positive OMPC. **Methods:** Eligible patients have histologically confirmed prostate cancer, biochemical recurrence post-definitive treatment, OMPC with ≤ 5 PSMA-positive metastatic lesions including ≥ 1 distant metastasis on PSMA PET/CT scans (all must be amenable to SBRT), PSA doubling time < 10 months and non-castration testosterone levels (> 100 ng/dL). Exclusion criteria include distant metastasis by conventional imaging (CI; CT/MRI and bone scans) at screening, prior ADT (except adjuvant ADT completed > 12 months before randomization), or other systemic therapy for metastatic prostate cancer. Patients (N = ~450) will be randomized 2:1 to ^{177}Lu-PSMA-617 or observation and will receive SBRT to all metastatic lesions within 14 days, completed within 3 weeks. Patients will then receive either intravenous ^{177}Lu-PSMA-617 (7.4 GBq/6 weeks; 4 cycles), starting 7–21 days after SBRT, or undergo observation only. Additional SBRT for new lesions is allowed. ADT is allowed after a metastasis-free survival (MFS) event by CI confirmed by blinded independent review committee (BIRC). Safety follow-up will occur 42 days after the last ^{177}Lu-PSMA-617 dose and at the week 24 visit for the observational arm. Long-term follow-up for the ^{177}Lu-PSMA-617 arm will include safety assessments every ~32 weeks. The primary endpoint is MFS by CI as assessed by BIRC using RECIST v1.1, or death. To provide 90% power to detect a hazard ratio of 0.6, 187 MFS events are required. The key secondary endpoint is time to next hormonal therapy. Additional secondary endpoints include time to PSA progression, radiographic progression-free survival, symptomatic progression, patient-reported health-related quality of life, overall survival and safety. Shore et al. PSMA-delay castration (DC): an open-label, multicenter, randomized phase 3 study of [^{177}Lu]Lu-PSMA-617 versus observation in patients with metachronous PSMA-positive oligometastatic prostate cancer (OMPC). J Urol 2025;213 (5S2_suppl):e28. https://www.auajournals.org/doi/10.1097/01.JU.0001110444.53548.eb. Reused with permission; ©American Urological Association, 2025. This abstract previously presented at 2025 AUA Annual Meeting. Clinical trial information: NCT05939414. Research Sponsor: Novartis.