TPS5121 Poster Session

A randomized phase 2 trial of flexible and extended dosing of ^{177}Lu-PSMA-617 molecular radioligand therapy in mCRPC (FLEX-MRT): Trial in progress update.

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Background: The U.S. Food and Drug Administration (FDA) approved ^{177}Lu-PSMA-617 radiopharmaceutical therapy (RPT) for patients with metastatic castration-resistant prostate cancer (mCRPC) with a fixed dosing schedule: Six cycles of 7.4 GBq administered in six-week intervals. However, a patient-tailored more flexible and extended dosing schedule of ^{177}Lu-PSMA RPT may increase treatment efficacy. In this randomized trial in men with mCRPC, we aim to determine the efficacy of a response-based flexible dosing schedule of ^{177}Lu-PSMA-617 RPT administered up to 12 treatment cycles compared to the current standard of care. **Methods:** This is an investigator-initiated prospective phase 2, open-label, randomized, controlled, parallel group, single-center trial. The aim is to assess the 2-year survival rate in mCRPC patients treated with a flexible dosing schedule of ^{177}Lu-PSMA RPT up to 12 cycles in comparison to the fixed dosing schedule of 6 cycles. Patients with progressive mCRPC post-ARSI, post taxane-based chemotherapy are eligible by PSMA positron emission tomography (PET) VISION trial criteria. Exclusion criteria include prior RPT and less than 6 weeks since the last myelosuppressive therapy. We hypothesized 2-year survival rates of 55% in the investigational group and 30% in the control group. A two-sided log rank test with an overall sample size of 90 subjects (45 treatment group, 45 control group) achieves 80.3% power at a 0.05 significance level to detect a hazard ratio of 0.050. Patients will be randomized in a 1:1 ratio: The investigational arm is treated with up to 12 cycles including potential "treatment holidays" depending on the treatment response (n=45); the control arm receives 6 cycles administered in six-week intervals (n=45). Imaging response to RPT is assessed using ^{177}Lu-PSMA-617 SPECT/CT after each cycle and PSMA PET/CT during treatment holidays (every 12 weeks), respectively. In the investigational arm, RPT will be re-started after a treatment holiday if the patient experiences a ≥25% PSA progression and an imaging progression according to the Response Evaluation Criteria in PSMA PET/CT (RECIP). Primary endpoint is the 2-year survival rate calculated from the date of the first cycle of RPT. Secondary endpoints include safety by Common Terminology Criteria for Adverse Events (CTCAE) and dosimetry, and determination of overall and progression-free survival (evidence of progression as defined by either radiographic, PSA, or clinical progression, or death from any cause). The FLEX-MRT trial has been approved by the FDA (IND #168362), and the UCLA IRB (#23-000931). The trial is registered on ClinicalTrials.gov (NCT06216249). The FLEX-MRT trial is currently recruiting. Start of enrollment was in August 2024. As of January 27th, 2025, 19 patients have been enrolled. Clinical trial information: NCT06216249. Research Sponsor: Prostate Cancer Foundation; Deutsche Forschungsgemeinschaft (DFG, German Research Foundation); 545058105; Novartis.