TPS5128 **Poster Session**

METANOVA: A phase II trial of metastasis-directed radiotherapy for de novo oligometastatic prostate cancer treated with long-term androgen deprivation therapy in the STAMPEDE trial.

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Background: Men with de novo oligometastatic hormone-sensitive prostate cancer (omHSPC) represent a unique subgroup where metastasis-directed radiotherapy (MDRT) may improve outcomes when added to systemic therapy. Retrospective data suggest potential survival benefits of MDT in oligometastatic prostate cancer (PCa), but prospective randomized evidence in the de novo setting is lacking. The METANOVA trial aims to determine whether MDRT, combined with standard systemic therapy (SST) and prostate-directed local therapy, improves outcomes for these patients. **Methods:** METANOVA is a phase II, randomized, open-label trial enrolling 200 men with histologically confirmed de novo omHSPC (NCT06150417). Oligometastatic disease defined as 1–5 metastatic sites by traditional imaging (MRI, CT, or ^{99m}Tc bone scan) or 1–10 sites by PSMA PET/CT. Patients are allowed up to 30 days of androgen deprivation therapy (ADT) prior to enrollment. Patients are randomized 1:1 to standard of care (SOC) or SOC + MDRT to all metastatic sites. SOC includes 12 months of SST (ADT, with addition of an androgen receptor signaling inhibitor; triplet therapy is not allowed) and definitive treatment of the primary. Planned local therapy may be prostate-directed radiation therapy with definitive dose (moderate hypofractionation and ultra-hypofractionation allowed) or radical prostatectomy (maximum 50 patients to receive surgery), determined prior to randomization. MDRT will be delivered using stereotactic body radiation therapy (SBRT) to all metastatic lesions on conventional imaging or PSMA PET/CT. Patients are stratified to the use of PSMA PET/CT to stage, number of bone metastasis (0 vs 1-3 vs 4-10), local treatment (RT vs RP), and plan to MDRT all sites of PSMA disease (yes vs no). The primary endpoint is failure-free survival (FFS), defined as the time from randomization to biochemical failure, local or distant progression, skeletal-related event, any salvage intervention after 12 months planned SOC therapy, or death from prostate cancer. Secondary endpoints include overall survival, radiographic progression-free survival, quality of life (EPIC-26 domains), and toxicity. Correlative studies will explore imaging and molecular features from the primary, metastasis, and circulating disease to develop a predictive biomarker of which patients would derive the greatest benefit from MDRT. This study is designed to demonstrate a 34% relative reduction in the hazard of FFS from the addition of MDRT to SOC, providing 80% power at a one-sided alpha level of 0.05. The trial activated in July 2024, aims to complete accrual within 3 years. Data from this trial is preplanned to be pooled with the STAMPEDE2 (NCT06320067) trial in the United Kingdom, which is assessing overall survival benefit of MDRT in men with de novo omHSPC. Funding: NIH U01CA257638. Clinical trial information: NCT06150417. Research Sponsor: NIH-NCI.