TPS5129 Poster Session

TRIPLE-SWITCH (SWOG/CCTG-PR26): A randomized phase III clinical trial for the addition of docetaxel to androgen receptor pathway inhibitors in patients with metastatic castration sensitive prostate cancer (mCSPC) and suboptimal PSA response (NCT06592924).

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Background: Management of patients (pts) with mCSPC remains a challenge due to its incurable nature and heterogeneous response to androgen deprivation therapy (ADT) and androgen receptor pathway inhibitors (ARPI). Recent analyses of phase III ADT + ARPI trials show that mCSPC with suboptimal PSA response (≥0.2ng/ml at 6-12 months) have poor prognosis, short time to castration-resistance (CRPC) and 30-36 month median overall survival (OS). While docetaxel could also be utilized in mCSPC, there is equipoise about its use in ARPI-treated pts because of 1) an absence of randomized data for docetaxel in this setting, 2) toxicity of docetaxel with impact on quality of life for pts, and 3) selection of docetaxel treatment by disease volume rather than disease biology. CCTG-PR26 (TRIPLE-SWITCH) is a joint CCTG-SWOG trial run through the NCI National Clinical Trials Network. This study investigates whether adding docetaxel prior to development of CRPC, regardless of disease volume, will improve OS in ARPI-treated mCSPC pts that show evidence of suboptimal response. **Methods:** This international, open-label, randomized phase III trial compares standard ADT + ARPI against the addition of docetaxel to ADT + ARPI in mCSPC pts with suboptimal PSA response, defined as PSA ≥0.2 ng/mL after 6-12 months of ADT and ≥4 months of ARPI. Stratification will be based on PSA levels, ARPI type, presence of liver metastasis, disease recurrence status, and time since ADT initiation. Arm 1 will continue standard ADT + ARPI (abiraterone acetate with prednisone, apalutamide, enzalutamide or darolutamide). Arm 2 will receive docetaxel 75mg/m^2 IV every 3 weeks for up to 6 cycles in addition to continuing standard ADT + ARPI. Sample size is 830 pts in order to detect a targeted 33% improvement in overall survival (hazard ratio 0.75) using a 1-sided 0.025 level test with 85% power. Key eligibility criteria are: ≥18 years, histologically confirmed prostate adenocarcinoma, metastatic disease present and confirmed by conventional imaging (CT and/or bone scan), PSA ≥5.0 ng/mL prior to ADT, receipt of ADT for 6-12 months and ARPI for ≥4 months, PSA ≥0.2 ng/mL within 14 days of enrolment, adequate organ and marrow function, ECOG performance status 0-2, eligible for docetaxel chemotherapy, no evidence of disease progression or biochemical progression on ADT prior to enrolment. Primary endpoint is overall survival. Secondary endpoints include PSA response, PSA kinetics, and clinical progression free-survival. Correlative studies will explore the prognostic and predictive value of circulating tumor DNA (ctDNA) and the association between molecular signatures in primary prostate cancer tissue and clinical outcomes. Enrolment has been initiated in January 2025 and is ongoing. Clinical trial information: NCT06592924. Research Sponsor: Canadian Institutes of Health Research; 195838; NCI National Clinical Trials Network (NCTN); CA180863; Canadian Cancer Society; 707213.