TPS5122 **Poster Session**

A randomized phase III trial investigating platinum and taxane chemotherapy in metastatic castration resistant prostate cancer (mCRPC) patients with alterations in DNA damage response (DDR) genes (OPTION-DDR) CCTG-PR-25 NCT06439225.

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Background: For patients (pts) with mCRPC there are numerous treatment options including single agent docetaxel after treatment with androgen receptor pathway inhibitors (ARPI). Despite the availability of varied treatments, overall survival (OS) for pts with mCRPC after ARPI remains poor (12-19 months). Improvements in outcomes are desperately needed. 25% of pts have alterations in DDR genes and are potentially sensitive to treatment with platinum agents. Carboplatin has been previously evaluated in smaller trials in pts with mCRPC and shows promise in patients with DDR gene alterations. PR-25 leverages standard of care testing for DDR genes to evaluate in a rigorous manner whether addition of carboplatin to docetaxel improves overall survival (OS) in pts with DDR gene alterations and mCRPC. **Methods:** PR25 is a phase III randomised controlled trial led by the Canadian Cancer Trials Group comparing docetaxel to docetaxel and carboplatin in pts with DDR alterations. Pts have to receive prior ARPI for mCRPC, and demonstrate radiographic or PSA progression prior to enrollment. Qualifying DDR gene alterations include: BRCA1, BRCA2, ATM, ATR, BRIP1, BARD1, CDK12, CHEK1, CHEK2, ERCC2, FANCA, FANCC, FANCD2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L. The primary endpoint is OS. Secondary endpoints include: radiographic progression free survival (PCWG3 and RECIST 1.1), PSA response, time to next systemic therapy, patient reported quality of life and economic evaluation. Statistical design: The target accrual is 236 patients over 3.25 yrs with 2 year follow-up to detect a HR of 0.65 in OS, using a 5% (2 sided) level test with power of 80%. Conduct to date: Study activation – October 2024. First patient enrolled - December 2024. Accrual to date: 2 Supported by CIHR grant #189966, NCTN grant #CA180863 and CCS grant #707213. Clinical trial information: NCT06439225. Research Sponsor: Canadian Institutes of Health Research; 189966; NCI's National Clinical Trials Network; CA180863; Canadian Cancer Society; 707213.