A phase II single arm prospective study of high dose testosterone in combination with carboplatin chemotherapy in late line metastatic castrate-resistant prostate cancer (HIGH-TeCH study).

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Background: Bipolar androgen therapy (BAT) is a safe and well-tolerated treatment paradigm in metastatic castrate resistant prostate cancer (mCRPC) but response rates and duration are modest. Preclinical data suggests supraphysiologic androgens interrupt DNA relicensing and increase double-stranded DNA breaks, suggesting a potential synergy with the addition of carboplatin chemotherapy. We assessed the safety and efficacy of this treatment combination in Arm B of the HIGH-TeCH trial. **Methods:** Men with refractory mCRPC after at least one line of taxane based chemotherapy and androgen signaling inhibitor received four weekly testosterone enanthate (500mg IM) with Carboplatin (AUC 5) and androgen deprivation therapy. Five (24%) PSA50 responses were achieved at planned interim analysis of the first 21 patients, meeting threshold for study expansion to a total of 40 participants. **Results:** Currently, 37 of a target total 40 patients have been recruited. Median follow up was 14.8 months as of 1st October 2024. Median age 72. Median prior lines of treatment 3; 51% of patients had prior 177-Lutetium. 27 patients discontinued treatment for disease progression (PSA, radiological, clinical), 1 discontinued due to a serious adverse event (CVA) and 9 patients remain on trial. Median of 5 cycles of BAT with Carboplatin were administered. Seven (19%) patients had a PSA response $\geq$ 50%. Fourteen (38%) patients had clinical benefit ($>$ 6 months duration on study). Median progression-free survival was 6.6 months (95% CI, 5.5 – 9.9). Median overall survival was 20.4 months (95% CI, 15.5 – not reached). Thirty-one (84%) patients experienced a treatment–related adverse event (TRAE); of which, 94% were grade 1 – 2. Highest rates of TRAEs were fatigue (52%), nausea (39%), musculoskeletal pain (23%), constipation (23%). There was no grade 4 TRAEs or deaths. **Conclusions:** BAT with carboplatin has an acceptable safety profile and demonstrated clinical benefit in heavily pre-treated mCRPC patients. Accrual will be completed imminently with final analysis to be presented. Translational studies to identify predictive biomarkers and quality of life analyses are underway. Clinical trial information: NCT00309985. Research Sponsor: Australian and New Zealand Urogenital and Prostate Cancer Trials Group; St. Vincent's Clinic Foundation Grant.