Comparison of outcomes with docetaxel or ARPI combination therapy for metastatic hormone sensitive prostate cancer (mHSPC) by volume of disease

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Background: Combination therapy has improved treatment of metastatic hormone sensitive prostate cancer (mHSPC). Doublets include androgen deprivation therapy (ADT) plus docetaxel (DOC) or the androgen receptor pathway inhibitors (ARPIs) abiraterone, enzalutamide, apalutamide, or darolutamide. There have been no large clinical trials that compare DOC to ARPIs in mHSPC. This study evaluates overall survival and time to castration-resistance in patients with de novo (synchronous) mHSPC in the Veterans Health Administration treated with combination therapy.

Methods: Veterans were identified with initial diagnosis of 'distant' prostate cancer. All veterans had ADT initiated within 4 months of diagnosis and followed until September 2023. First combination therapy with DOC from 7/2016-6/2021 or ARPI from 7/2017-6/2021 were included if initiated within 4 months after ADT. Volume of disease was determined from chart review and castration-resistance (mCRPC) by a combination of natural language processing and administrative data. Real-world progression-free survival (rwPFS) was determined as time to mCRPC or death. Kaplan-Meier time to event analyses and Cox proportional hazard modeling with age, Black race, Charlson comorbidity index, prostate specific antigen, body mass index, and weight change in the year prior was used for analyses.

Results: 1,226 patients with de novo mHSPC were identified with median age of 71.5 years and 349 (28.6%) were Black. High volume disease was identified in 929 (76.0%) and low volume in 293 (24.0%). DOC was used in 341 (27.9%) and ARPIs in 881 (72.1%). Veterans with high volume disease had shorter overall survival (OS) than low volume (23.8 vs. 64.1 months, $p<0.001$). Overall, there was no difference in OS between DOC and ARPI (36.4 vs. 38.9 months, $p=0.68$), however DOC was associated with a shorter rwPFS (16.5 vs 22.1 months, $p<0.001$). In high volume disease, there was no difference in OS between DOC and ARPI (33.8 vs. 32.5 months, $p=0.68$), however DOC was associated with a shorter rwPFS (14.9 vs 19.2 months, $p=0.002$). In a multivariable model of patients with high volume disease, there was no difference in OS observed between initial treatment with DOC and ARPIs (aHR 0.83, 95% CI 0.69-1.00).

Conclusions: In veterans with de novo mHSPC, no difference in OS were observed between combination treatment with DOC or ARPI in patients with low or high-volume mHSPC. ARPIs were associated with longer progression free survival. Due to a lack of clinical trials comparing DOC and ARPI therapy, these data may guide selection of combination therapy for mHSPC.

Table 1: Time in months to rwPFS or death in veterans with synchronous mHSPC

	Low volume n=293		High Volume n=929	
Treatment	rwPFS (mos)	Overall Survival (mos)	rwPFS (mos)	Overall Survival (mos)
ADT+docetaxel n=341	24.3	64.5	14.9	33.8
ADT+ARPI n=881	41.9	67.4	19.2	32.5
Total n=1222	37.3	64.5	17.2	33.0

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