# Outcomes of First-Line Abiraterone Acetate or Enzalutamide for Older Adults With Metastatic Castration-Resistant Prostate Cancer According to Use of Upfront Docetaxel for Metastatic Castration-Sensitive Prostate Cancer in an International Multicenter Registry: A SPARTACUSS—Meet-URO 26 Study

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## Abstract

**This study evaluates treatments for metastatic castration-resistant prostate elderly (aged ≥ 75). Analyzing 337 patients, no significant difference in survival or safety have been found between patients treated with abiraterone acetate plus prednisone or enzalutamide, regardless of prior docetaxel use. This suggests similar efficacy and tolerability in a population of patients with limited clinical data.**

**Background:** Managing metastatic castration-resistant prostate cancer (mCRPC) in men aged ≥ 75 is challenging due to limited data. Regardless of age, in real-world clinical practice, most mCRPC still derive from failure of androgen deprivation therapy (ADT) with or without docetaxel (D) for metastatic castration-sensitive prostate cancer (mCSPC). As

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abiraterone acetate plus prednisone (AA) and enzalutamide (Enza) are common first-line treatments for mCRPC. The impact of prior use of D for mCSPC on the efficacy and safety of AA or Enza in this older population remains unclear. **Methods:** A cohort of patients aged ≥ 75 years starting AA or Enza as first-line therapy for mCRPC from January 2015 to April 2019 was identified from the registries of 10 institutions. Patients were categorized into 2 groups based on previous use of D for mCSPC. Primary endpoints were cancer-specific survival (CSS) from AA or Enza start, CSS from ADT onset, and safety. We used Kaplan–Meier method to estimate the endpoints distribution, including median values with 95% confidence intervals (95% CI). **Results:** Of the 337 patients identified, 24 (7.1%) received ADT+D and 313 (92.9%) received ADT alone for mCSPC. Median follow-up from AA/Enza start was 18.8 months. Median CSS from ADT or AA/Enza was not significantly different between ADT+D and ADT alone cohorts (71.9 vs. 52.7 months, $P = .97$; 25.4 vs. 27.2 months, $P = .89$, respectively). No statistically significant difference in adverse events (AEs) of any grade rate (58.3% vs. 52.1%, respectively; $P = .67$) or grade ≥ 3 (12.5% vs. 15.7%, respectively; $P = 1.0$) was found between ADT+D and ADT alone cohorts. **Conclusions:** Despite the innate limitations of a retrospective design and relatively small size of the ADT+D cohort, this analysis suggests that elderly men receiving AA or Enza as first-line therapy for mCRPC have similar survival outcomes and tolerability, regardless of previous D for mCSPC.

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**Keywords:** ARSi, Chemotherapy, Elder population, mCRPC, Safety

## Introduction

Almost one third of all new cases of prostate cancer (PCa) are diagnosed in senior men aged ≥75 years.[1] PCa is the second leading cause of cancer mortality in the elderly patient and approximately two thirds of all PCa deaths occur in men ≥ 75 years old.[2,3] In fact, elderly patients are more likely to be diagnosed with an advanced stage of disease compared to younger patients (< 75 years) and are often frailer due to their burden of comorbidities and higher susceptibility to treatment toxicities.[4,5] As such, the optimal management of PCa in this age group is both paramount and challenging, especially due to the limited clinical data on this population available in the literature.[6] This holds particularly true for the final stage of the disease, termed metastatic castration-resistant PCa (mCRPC), defined as biochemical progression (per Prostate Cancer Working Group 3 definition; PSA increase ≥ 25% of nadir and at least ≥ 1 ng/mL, confirmed by a second rise at ≥ 1 week-interval), radiographic or clinical progression during ADT, despite castrate levels of testosterone (< 50 ng/dL), which is incurable and associated with poor prognosis.[7,8]

Over the past decade, the positive findings of pivotal randomized controlled trials have led to the approval of combinations of the traditional androgen-deprivation therapy (ADT) with docetaxel chemotherapy and androgen-receptor signaling inhibitors (ARSi), such as abiraterone acetate plus prednisone (AA), enzalutamide (Enza), darolutamide, and apalutamide for metastatic castration-sensitive disease (mCSPC).[8,9] Despite ADT + ARSi being standard of care for mCSPC and strongly recommended in this setting by international guidelines,[8,9] recent real-world evidence studies showed that most patients with mCSPC, particularly older adults, still receive ADT alone.[10,11,12] This underutilization may be the result of logistic issues or the physician's choice based on older patients' frailty status. Although the number of patients receiving intensified treatment for mCSPC will likely grow in time, AA and Enza are still the most frequently used first-line therapies for mCRPC in current clinical practice.[13,14,15] Nevertheless, it is unclear whether use of upfront docetaxel for mCSPC may impact their clinical efficacy or safety in men aged 75 years or older. Therefore, the present analysis seeks to retrospectively evaluate the efficacy and tolerability of AA or Enza as first-line therapy for mCRPC in this elderly population, classified by use of docetaxel for mCSPC.

## Methods

The SPARTACUSS (prostate cancer specific population-directed androgen receptor targeted agents in North America, Canada, European Union, Switzerland, South America) cohort study adhered to the strengthening the reporting of observational studies in epidemiology (STROBE) reporting guidelines. This retrospective study involved 10 institutions across Italy, France, Switzerland, Canada, USA, and Brazil. Prior to initiating data collection, an institutional review board approval was obtained in each center and informed consent was waived due to all data being de-identified. The clinical and electronic registries of the 10 participating centers were used to identify a cohort of consecutive patients who received AA or Enza as first-line therapy for histologically confirmed and radiologically evident mCRPC between January 1, 2015 and April 1, 2019. Patients who had received life-prolonging therapies prior to AA or Enza, with the exception of ADT, ADT plus docetaxel, or ADT plus radiotherapy, were excluded from the analysis. Date of data cut-off was April 1, 2022. Detailed description of the study methods for all SPARTACUSS studies can be found in previous publications.[16,17]

In this analysis, patients were included if aged ≥ 75 years, the same age cut-off used by the International Society of Geriatric Oncology (SIOG) guidelines,[18] when starting AA or Enza as first line therapy for mCRPC and were classified according to receipt of upfront docetaxel for mCSPC. The primary endpoints were cancer-specific survival (CSS) from ADT start and CSS from AA or Enza start, defined as record interval from ADT or AA/Enza initiation, respectively, to demise from PCa and safety, described by analysis of

adverse events (AEs) in both cohorts and graded according to the Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 5.0. The secondary endpoint was radiographic progression free survival (rPFS), defined as the record time from AA/Enza start to the first documentation of radiographic tumor progression (according to according to the Response Evaluation Criteria in Solid Tumors criteria, version 1.1)[19] or censored at last follow-up visit or death from any cause, whichever occurred first. The distribution of endpoints, including median time-to-event and its 95% confidence interval (CI), was estimated with Kaplan–Meier method. The log-rank test was used to compare time-to-event distributions among the cohorts with estimates of hazard ratio and Cox regression analysis was performed to estimate specific Hazard Ratio (HR), with corresponding 95% Confidence Intervals (CI). The Mann–Whitney *U* test was utilized to compare continuous variables, and chi-square test for categorical variables. Statistical analyses were performed using SPSS Statistics software (Statistical Package for Social Sciences, SPSS Statistics, IBM Corporation, Armonk, NY; version 22).

## Results

Overall, this analysis included 337 eligible patients with a median age of 80 years at initiation of ARSI. Of these, 24 patients (7.1%) received ADT in combination with docetaxel and 313 (92.9%) had ADT alone for mCSPC. Median follow-up from ADT start was 39.0 months (95% CI, 34.7-41.2 months), median follow-up from AA/Enza start was 18.8 months (95% CI, 17.0-19.8 months). Baseline patient characteristics are summarized in Table 1. Patients treated with ADT + docetaxel were significantly younger compared to the ADT alone group (median age 78 vs. 81 years, respectively; $P = .022$). Although not statistically significant, the subgroup treated with docetaxel also displayed higher rates of Gleason score $\geq 8$ (81.0% vs. 62.6%, $P = .10$), de-novo metastatic disease (83.3% vs. 65.6%, $P = .08$) and high-volume (HV) disease (45.8% vs. 34.6%, $P = .28$), per CHAARTED trial definition,[20] compared to those treated with ADT alone. No significant difference in median CSS from ARSi start was observed between the ADT + docetaxel cohort and the ADT alone cohort (25.4 vs. 27.2 months; HR = 0.96; 95% CI, 0.52-1.76; $P = .89$) (Table 2). Median CSS from ADT start was not statistically different in the ADT + docetaxel and ADT alone cohorts (71.9 vs. 52.7 months; HR = 0.99, 95% CI, 0.54-1.82; $P = .97$) (Table 2). The specific cause of death was not available for 2 patients (1 in each cohort) who were consequently excluded from this analysis. The Kaplan-Meier estimates of CSS remark these findings showing largely overlapping curves (Figure 1). The 2 cohorts also showed comparable median rPFS (16.6 vs. 19.4 months, respectively; HR = 0.95, 95% CI, 0.53-1.71; $P = .86$) (Table 3).

No statistically significant difference was found in the incidence of AEs of any grade (58.3% vs. 52.1%, respectively; $P = .67$) or grade $\geq 3$ (12.5% vs. 15.7%, respectively; $P = 1.0$) between ADT + docetaxel and ADT alone cohorts (Table 4). Similarly, the rates of dose reduction ($P = .33$) and treatment discontinuation ($P = .55$) did not statistically differ in the 2 cohorts (Table 4). AEs of any grade and of grade $\geq 3$ are detailed in Supplemental Tables 1 and 2, respectively.

## Discussion

A significant segment of PCa patients comprises individuals aged 75 years or older. This population is quite heterogeneous since chronological age often inadequately reflects overall clinical status. A more profound comprehension of patient frailty becomes fundamental in avoiding both undertreatment and overtreatment.[21] In this perspective, various validated tools (ie, Charlson Comorbidity Index, Mini-Cog screen and G8 score) allow for an accurate geriatric evaluation and could help the clinician in tailoring therapy for older men with PCa.[22,23] Although the use of these indicators is strongly recommended by international ad-hoc task forces, they are still not commonly applied in clinical practice.[24] As such, also considering the lack of grade 1 evidence for this age-specific population with PCa, real-world evidences acquire a great relevance in providing guidance for the decision-making process. In this regard, although a retrospective analysis assessed the clinical impact of upfront docetaxel on subsequent first-line AA or Enza for mCRPC in an age unspecified population,[25] to the best of our knowledge, this is the first report to specifically describe the efficacy and tolerability of first-line AA or Enza for men $\geq 75$ years old with mCRPC progressing after early docetaxel for mCSPC.

In this real-world evidence intercontinental multicenter analysis, senior adults aged 75 years or more treated with AA or Enza as first line therapy for mCRPC showed similar survival outcomes regardless of previous use of docetaxel for mCSPC. Interestingly, most patients in the ADT + docetaxel cohort had poor prognostic factors such as GS $\geq 8$ (81.0%), de novo metastatic disease (83.3%), and ECOG PS $\geq 1$ (78.3%) and the whole cohort was younger (median age 78 years vs. 81 years) and tended to exhibit higher rates of poor prognostic variables in comparison with the ADT alone cohort. As the addition of docetaxel to ADT for mCSPC is known to work best on those with worse prognosis,[26] these observations could partly explain the clinician's choice to use antiblastic therapy upfront in these patients and maybe the numerical advantage of nearly 20 months (71.9 vs. 52.7 months) of CSS from ADT onset achieved in the ADT + docetaxel cohort with respect to the ADT alone cohort. However, this presumptive benefit was not confirmed by the CSS from ARSi start analysis. In fact, those who received upfront D had similar CSS from ARSi start compared to those who had ADT alone (25.4 vs. 27.2 months) and these survival data align with the median overall survival achieved in subanalyses of the elderly ($\geq 75$ years old) population of clinical trials investigating Enza or AA as first-line therapy for mCRPC.[27,28]

In terms of safety, rates of AEs of any grade as well as of grade $\geq 3$ were similar between the 2 groups and only in 2 cases (8.3%) in the ADT + docetaxel group and in 46 cases (14.7%) in the ADT alone group a discontinuation due to toxicity became necessary. These findings are relevant considering that the elderly population is particularly prone to developing AEs due to comorbidities and polypharmacy.[23,24,29] Further, it is in line with what showed in a post-hoc analysis of the CHAARTED trial where older men (> 70 years) treated with ADT + docetaxel had similar safety outcomes compared to younger men (< 70 years old).

Main limitations to this analysis are the retrospective design of the study, which inherently introduces certain biases, and the absence of a comprehensive geriatric assessment, which may not capture

**Table 1** Patient Characteristics

| Variable | Overall (n = 337) N (%) | ADT+D (n = 24) N (%) | ADT Alone (n = 313) N (%) | *P*-Value[a] |
|---|---|---|---|---|
| Median age at start of ARSi, yrs (IQR) | 80 (77.5-84.0) | 78 (76-82) | 81 (78-84) | **.022** |
| Race (NA:132) | | | | |
| Caucasian | 183 (89.3) | 14 (82.4) | 169 (89.9) | **.034** |
| Black | 9 (4.4) | 3 (17.6) | 6 (3.2) | |
| Hispanic | 5 (2.4) | 0 (0) | 5 (2.7) | |
| Asian | 8 (3.9) | 0 (0) | 8 (4.2) | |
| Gleason score (NA: 94) | | | | |
| ≤ 7 | 87 (35.8) | 4 (19.0) | 83 (37.4) | |
| 8+ | 156 (64.2) | 17 (81.0) | 139 (62.6) | .10 |
| Prior local therapy with curative intent (NA:1) | | | | |
| No | 218 (64.9) | 17 (70.8) | 201 (64.4) | |
| Surgery | 73 (21.7) | 2 (8.3) | 71 (22.8) | |
| Radiotherapy | 45 (13.4) | 5 (20.9) | 40 (12.8) | .19 |
| Time of metastatic presentation (NA:2) | | | | |
| Prior local therapy with curative intent | 111 (33.1) | 4 (16.7) | 107 (34.4) | |
| De novo | 224 (66.9) | 20 (83.3) | 204 (65.6) | .08 |
| Volume at M1 (NA:7) | | | | |
| Low | 213 (64.5) | 13 (54.2) | 200 (65.4) | .28 |
| High | 117 (35.5) | 11 (45.8) | 106 (34.6) | |
| ECOG PS at start of ARSi (NA:22) | | | | |
| 0-1 | 243 (77.1) | 17 (73.9) | 226 (77.4) | .80 |
| > 1 | 72 (22.9) | 6 (26.1) | 66 (22.6) | |
| Median PSA at start of ARSi (NA:12) ng/mL (IQR) | 22.8 (6.7-92.1) | 14.4 (3.23-34.6) | 23.83 (6.94-95.3) | .13 |
| Type of metastases at start of ARSi (NA:4) | | | | |
| Lymph nodes only | 33 (9.9) | 1 (4.2) | 32 (10.4) | |
| Bone and/or lymph nodes | 264 (79.3) | 20 (83.3) | 244 (79.0) | |
| Visceral except for liver, and/or bone/lymph nodes | 30 (9.0) | 2 (8.3) | 28 (9.1) | .63 |
| Liver and/or other visceral, bone, lymph nodes | 6 (1.8) | 1 (4.2) | 5 (1.5) | |
| Median FU from ARSi onset, mos (95% CI) | 18.8 (17.0-19.8) | 14.6 (7.7-18.1) | 18.9 (17.0-19.9) | .16 |
| Median FU from ADT onset, mos (95% CI) | 39.0 (34.7-41.2) | 33.4 (21.6-39.4) | 39.1 (34.8-41.4) | .40 |

Abbreviations: ADT = androgen deprivation therapy; ARSi = androgen receptor signaling inhibitors; CI = confidence interval; D = docetaxel; ECOG PS = Eastern Cooperative Oncology Group performance status; FU = follow-up; IQR = interquartile range; mos = months; N = number; NA = not available; yrs = years.
[a] *P*-value from Mann–Whitney U test or chi-square test, as appropriate.
*P*-value in bold if ≤ to 0.05.

**Table 2** Cancer-Specific Survival According to Use of D for mCSPC

| Cohort | N. (%) | N. of Deaths (%) | Median CSS From ADT Start, mos (95% CI) | HR (95% CI) | *P*-Value | Median CSS From ARSi Start, mos (95% CI) | HR (95% CI) | *P*-Value |
|---|---|---|---|---|---|---|---|---|
| ADT+ D | 23 (6.9) | 11 (47.8) | 71.9 (15.4 -128.3) | 1 (ref) | 0.97 | 25.4 (12.1-38.6) | 1 (ref) | .89 |
| ADT alone | 312 (93.1) | 176 (56.4) | 52.7 (43.9-61.5) | 0.99 (0.54-1.82) | | 27.2 (24.7-29.8) | 0.96 (0.52-17.6) | |

Abbreviations: AA = abiraterone acetate; ADT = androgen deprivation therapy; ARSi= androgen-receptor signaling inhibitors; CI = confidence interval; CSS = cancer-specific survival; D = docetaxel; E = enzalutamide; HR = hazard ratio; mos= months; N = number.

the full spectrum of frailty for every patient. Besides, the relatively short follow-up, unbalanced characteristics of the 2 cohorts and the small sample size of patients treated with docetaxel may have impacted the robustness of the findings. However, it should be noted that the latter limitation is reflective of the current clinical practice where most patients, especially if elderly, are still treated with ADT alone and only a few receive intensified treatment with upfront docetaxel for mCSPC.[10,11] Also, the added value of this study is given by patients' clinical characteristics, with the majority showing an ECOG PS ≥ 1 (71.1%) and almost all having at least 1 comor-

**Figure 1** Kaplan–Meier curves of cancer-specific survival from ARSi start (panel A) and cancer-specific survival from ADT start (panel B) according to use of D for mCSPC: AA = abiraterone acetate; ARSi = androgen-receptor signaling inhibitors; ADT = androgen-deprivation therapy; CSS = cancer-specific survival; D = docetaxel; E = enzalutamide; N = number.

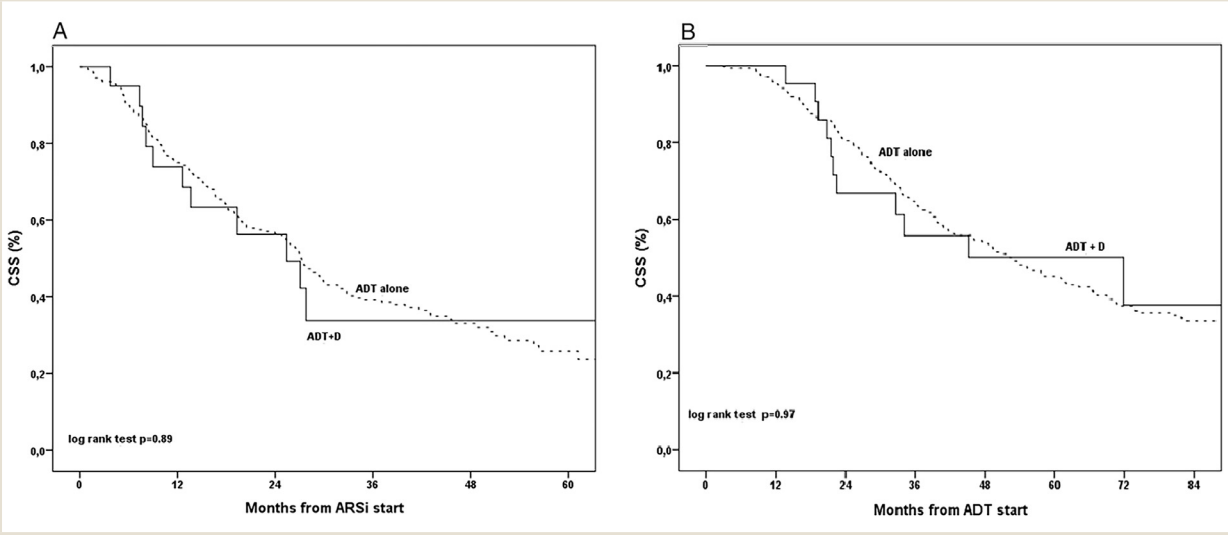


**Table 3** Radiographic Progression-Free Survival According to Use of D for mCSPC

| Cohort | N. (%) | Median rPFS From ARSi Start, mos (95% CI) | HR (95% CI) | *P*-Value |
|---|---|---|---|---|
| ADT+ D | 24 (7.1) | 16.6 (6.0-27.1) | 1 (ref) | .86 |
| ADT alone | 313 (92.9) | 19.4 (15.7-23.0) | 0.95 (0.53-1.71) | |

Abbreviations: AA = abiraterone acetate; ADT = androgen deprivation therapy; ARSi= androgen-receptor signaling inhibitors; CI = confidence interval; D = docetaxel; E = enzalutamide; HR = hazard ratio; N = number; mos = months; rPFS radiographic progression-free survival.

**Table 4** Safety of ARSi According to Use of D for mCSPC

| | ADT + D N (%) | ADT Alone N (%) | Overall N (%) | *P*-Value[a] |
|---|---|---|---|---|
| AE any grade | | | | |
| No | 10 (41.7) | 150 (47.9) | 160 (47.5) | .67 |
| Yes | 14 (58.3) | 163 (52.1) | 177 (52.5) | |
| AE grade ≥ 3 | | | | |
| No | 21 (87.5) | 264 (84.3) | 285 (84.6) | 1.0 |
| Yes | 3 (12.5) | 49 (15.7) | 52 (15.4) | |
| Rx dose reduction | | | | |
| No | 23 (95.8) | 274 (87.5) | 297 (88.1) | .33 |
| Yes | 1 (4.2) | 39 (12.5) | 40 (11.9) | |
| Rx discontinuation | | | | |
| No | 22 (91.7) | 267 (85.3) | 289 (85.8) | .55 |
| Yes | 2 (8.3) | 46 (14.7) | 48 (14.2) | |

Abbreviations: AE = adverse event; ADT = androgen-deprivation therapy; D = docetaxel; N = number; Rx = treatment.
[a] *P*-value from fisher exact test.

bidity (91.5%), hence representing a convincing real-world elderly population.

Notably, the study offers insights into a demographic often overlooked in clinical research. It highlights that age alone should not be the sole determinant of treatment decisions, and further considerations such as patient frailty and comorbidities need to be factored into clinical decision-making. In this respect, the ongoing phase 3 trial PEACE-6 (NCT04916613) is investigating the efficacy and safety of ADT with or without darolutamide in frail patients with mCSPC who are not eligible for docetaxel or other ARSi and its

prospective data may shed more light over this challenging population.

## Conclusion

Despite the innate limitations to this report including the short median follow-up, the small number of patients and the retrospective nature, this intercontinental multicenter real-world analysis suggests that in a population of elderly patients aged 75 years or more with heterogenous characteristics, AA or Enza used as first-line therapy for mCRPC have comparable efficacy and tolerability regardless of prior use of docetaxel for mCSPC. Although these findings need validation through large prospective clinical trials or systematic meta-analyses, they may aid the physician's treatment decision process for the elderly patient with PCa and encourage further prospective studies aimed at optimizing treatment approaches for this group of patients.

### *Clinical Practice Points*

- Managing metastatic castration-resistant prostate cancer (mCRPC) in elderly men is challenging due to limited clinical data. Abiraterone acetate plus prednisone (AA) and enzalutamide (Enza) are common first-line treatments in this setting, but the impact of prior docetaxel (D) use on their efficacy and safety in older patients remains unclear.
- This study found no significant differences in cancer-specific survival or safety between elderly patients, defined as aged 75 years or more, treated with AA or Enza, regardless of prior use of docetaxel. This suggests that these treatments are similarly effective and well-tolerated in this population.
- The findings can help inform treatment decisions for elderly mCRPC patients, providing reassurance that AA and Enza are viable options even if docetaxel was used previously. This could lead to more personalized and effective treatment plans, improving patient outcomes.

## Disclosure

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## CRediT authorship contribution statement

**Giuseppe Fotia:** Conceptualization, Writing – original draft, Writing – review & editing. **Calogero Saieva:** Formal analysis, Methodology, Writing – review & editing. **Richard Lee-Ying:** Investigation, Writing – review & editing. **Anna Patrikidou:** Investigation, Writing – review & editing. **Pier Vitale Nuzzo:** Investigation, Writing – review & editing. **Elisa Zanardi:** Investigation, Writing – review & editing. **Sabrina Rossetti:** Investigation, Writing – review & editing. **Matthew Davidsohn:** Investigation, Writing – review & editing. **Marc Eid:** Investigation, Writing – review & editing. **Talal El Zarif:** Investigation, Writing – review & editing. **Heather McClure:** Investigation, Writing – review & editing. **Gian Paolo Spinelli:** Investigation, Writing – review & editing. **Alessandra Damassi:** Investigation, Writing – review & editing. **Veronica Murianni:** Investigation, Writing – review & editing. **Charles Vauchier:** Investigation, Writing – review & editing. **Thiago Martins Oliveira:** Investigation, Writing – review & editing. **Andrea Malgeri:** Investigation, Writing – review & editing. **Mikol Modesti:** Investigation, Writing – review & editing. **Ricardo Pereira Mestre:** Investigation, Writing – review & editing. **Loana Valenca:** Investigation, Writing – review & editing. **Praful Ravi:** Investigation, Writing – review & editing. **Daniele Santini:** Investigation, Writing – review & editing. **Sandro Pignata:** Investigation, Writing – review & editing. **Ugo De Giorgi:** Investigation, Writing – review & editing. **Christopher Sweeney:** Investigation, Writing – review & editing. **Daniel Heng:** Investigation, Writing – review & editing. **Giuseppe Procopio:** Investigation, Writing – review & editing. **Antonio Russo:** Investigation, Writing – review & editing. **Edoardo Francini:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

## IRB Approval

The present study was conducted according to the World Medical Association Declaration of Helsinki. An institutional review board approval was achieved in each center prior to commencing data collection and a waiver of informed consent was granted owing to all data being de-identified.

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## Supplementary material

**Supplemental Table 1. Adverse Events of Any Grade According to Use of Docetaxel for Metastatic Castration-Sensitive Prostate Cancer**

| Adverse Events of Any Grade[a] | ADT + D N (%) | ADT Alone N (%) | Overall N (%) |
|---|---|---|---|
| No adverse events of any grade | 11 (44.0) | 183 (51.0) | 194 (50.5) |
| Asthenia | 9 (36.0) | 71 (19.8) | 80 (20.8) |
| Hypokalemia | 1 (4.0) | 4 (1.1) | 5 (1.3) |
| Hypertension | 1 (4.0) | 6 (1.7) | 7 (1.8) |
| Liver dysfunction | 1 (4.0) | 11 (3.1) | 12 (3.1) |
| Cardiac disorders | 0 | 14 (3.9) | 14 (3.6) |
| Fluid retention | 0 | 18 (5.0) | 18 (4.7) |
| Gastrointestinal symptoms | 1 (4.0) | 20 (5.6) | 21 (5.5) |
| Urinary symptoms | 1 (4.0) | 17 (4.7) | 18 (4.7) |
| Falls | 0 | (4.2) | 15 (3.9) |

Abbreviations: ADT = androgen-deprivation therapy; D = docetaxel; N = number.
[a] NA = not available data for 18 patients (2 ADT+D, 16 ADT alone).

**Supplemental Table 2. Adverse Events of Grade ≥ 3 According to Use of Docetaxel for Metastatic Castration-Sensitive Prostate Cancer**

| Adverse Events of Grade 3[a] | ADT + D N (%) | ADT Alone N (%) | Overall N (%) |
|---|---|---|---|
| No adverse events of grade ≥ 3 | 16 (84.1) | 262 (85.2) | 278 (85.0) |
| Asthenia | 1 (5.3) | 19 (6.2) | 20 (6.1) |
| Hypokalemia | 1 (5.3) | 0 | 1 (0.3) |
| Hypertension | 0 | 0 | 0 |
| Liver dysfunction | 1 (5.3) | 1 (0.3) | 2 (0.6) |
| Cardiac disorders | 0 | 9 (2.9) | 9 (2.8) |
| Fluid retention | 0 | 2 (0.6) | 2 (0.6) |
| Gastrointestinal symptoms | 0 | 7 (2.3) | 7 (2.1) |
| Urinary symptoms | 0 | 2 (0.6) | 2 (0.6) |
| Falls | 0 | 6 (1.9) | 6 (1.9) |

Abbreviations: ADT = androgen-deprivation therapy; D = docetaxel; N = number.
[a] NA = not available data for 59 patients (8 ADT+D, 51 ADT alone).